Vol. 22, No. 4 April, 1925

THE
PSYCHOLOGICAL BULLETIN

EMOTION AND ENDOCRINE ACTIVITIES

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The endocrine glands have so close relation to the mind that no mental process can be completely free from endocrine influence in some way or other. Many hypotheses and guesses are current among students of endocrinology, but here it is endeavored to consider and evaluate the facts as far as possible with little heed to the fancies.

The term "endocrine" is adopted for indicating a gland with internal secretion; "hormone" for the active substance of the gland including both those of exciting and of inhibitory nature. "Autonomic nervous system" is used for the involuntary nervous system; "sympathetic" for the part of the autonomic as emerging in the thoracic-lumbar region of the spinal cord; and "parasympathetic" indicating the cranial and sacral parts of the autonomic. The main reason for the adoption of these terms is for convenience and custom, and the same is true of the other terminology used.

We have shown that the emotions are expressed in bodily changes, in the main, through sympathetic innervation, and that the chief endocrine organs so far as we know are brought into action by the nervous impulses by way of the fibers belonging to the sympathetic domain. From these facts it is to be expected that the emotions would stimulate the endocrine organs to extra activities and these endocrine activities would contribute to emotional somatic expressions. The vast significance of the elucidation of this problem for the widespread field of science, hygiene and culture hardly needs to be mentioned. But this is by no means an easy task.

Although the pioneer work of Dr. Cannon on a part of this subject first appeared in 1911, and this specific problem has been eagerly

discussed on the basis of laboratory experiments by prominent physiologists corroborating or contradicting Cannon, general agreement has not yet been attained. As regards most of the other glands our knowledge is too vague even to arouse much argument among investigators. The importance of the task, however, is so great that we urgently wish to know anything available in regard to the problem.

The relation of the emotional and endocrine activities has two phases; first, the influence of emotion on the endocrines; and second, the influence of the endocrines in arousing emotion. These two will now be considered:

1. The Emotional Influence on the Endocrine Activity

A. The Adrenal Gland

We have no definite information about the secreting mechanism of the adrenal cortex; our knowledge in this connection is confined to the medulla.

The work of Cannon and de la Paz on this subject seems to have already become classic, and it is hardly necessary to state it here except for criticism.

An isolated strip of rabbit intestine muscle, previously known as a sensitive indicator of adrenalin, was used in this experiment as the test object which was rhythmically contracting in a glass cylinder containing oxygenated Ringer's solution at body temperature. Minute doses of adrenalin were used to inhibit the contraction. Cats, excited when barked at by a dog while they were fastened in a holder, "presented the typical picture with scarcely a movement of defense" (14, p. 44). In each case samples of blood were taken by a long catheter from exactly the same region of the body—the inferior vena cava near the lumbar adrenal veins—before and after the barking. Blood from the quiet normal animal, or that taken before the excitement, produced no relaxation of the intestine strip. On the other hand, blood from the animal which showed emotional excitement, evoked the characteristic inhibition. In some instances the rate of inhibition was paralleled by the length of exciting time (14, p. 55). That the inhibition was due to an increased adrenal secretion was inferred from the following facts:

(1) The effect was produced only by "excited" blood from the neighborhood of the adrenal veins, while the blood from the femoral vein or from the kidneys had no such property.

(2) Excitement four or five hours after the removal of the adrenal glands did not alter the blood and cause the typical inhibition, though the animal showed "all the characteristic signs" of emotion.

(3) All variation of inhibitory action of the "excited" blood was duplicated by adding to inactive blood varying amounts of adrenalin.

(4) The effective blood lost its inhibitory power after three hours of exposure to bubbling oxygen. This same procedure is known as the one for destruction of adrenalin.

From these facts the conclusion was drawn by the authors that "the characteristic action of adrenin on intestinal muscle was in fact . . . due to secretion of the adrenal glands, and that that secretion is increased in great emotion" (14, p. 59).

These considerations justify us in attributing the secretion of adrenalin to emotion, for the animals, as above cited, showed the typical picture of excitement without marked muscular exertion.

No evidence, however, that adrenalin thus increased is poured out into the general circulation of the blood and consequently acts on the various organs of the body, was brought forth in these experiments. On the contrary, they rather tend to show the reverse, which gave Gley the opportunity to attack and deprive Cannon of the most important credit for his experiments.

The experiments of Hitchings, Sloan and Austin, on cats, cited by Cannon, and Crile's tests on rabbits and cats (30, p. 147) all confirmed Cannon's results, using his method. But apparently the above question raised by Gley was still left unsolved. Moreover, Stewart and Rogoff (93) failed to obtain positive results by the method of Cannon and de la Paz. "It may be stated, however," said Cannon, (15, p. 406) "that the method is difficult and exacting, and that not until after some experience with it did it begin to yield us positive result."

Eventually, however, Cannon found a simpler and more unmistakable method. A denervated heart, in the body of the animal experimented upon, which is a highly sensitive organ to adrenalin, was made use of as an indicator. Besides many important advantages enumerated by himself (15, p. 407), this method serves also for solving the question as to the adrenalin outflow into the general blood stream in consequence of emotional excitement. The stellate ganglia, the right vagus nerve, and the left vagus nerves were cut at intervals (no time is stated). The heart thus completely disconnected

from the central nervous system, no agency but through the blood can exert its influence on the heart beat. The graphic record of the heart beat showed that in a cat with the intact adrenal glands the rate was 217 beats per minute when the animal was calm, and 255 when excited. Two days after the bilateral adrenalectomy the rate was just the same as before removal when the cat was tranquil, 217. In three minutes it rose to 221 by excitement (15, pp. 414–415). Here no detail was stated about the manner of exciting the animal, yet presumably the same procedure as in his earlier experiment was used. Objections were raised against this result's being taken as the evidence of emotional increase of adrenalin output, by Stewart and Rogoff, for the reason that the faster beating of the denervated heart can be explained by a "redistribution of blood in the body" (94, 95).

This objection was put to test by Cannon and Rapport. They found that, even though all possibilities of redistribution were previously prevented by tying the blood vessels and severing the nerves, the more rapid beat could be elicited by stimulating the afferent nerve, which, according to Cannon, exerts the same influence on the adrenal glands as emotional excitement, so that is to be taken as a representative stimulus (21, p. 308). At the same time they found that the residual reflex acceleration of the heart after adrenalectomy (for which reason Stewart and Rogoff denied its dependence upon the adrenalin increase) was chiefly due to some unknown secretion from the liver. Excluding this factor by cutting the hepatic nerve, Cannon and Carrasco again confirmed that the adrenalin increase is responsible for the accelerated beat of the denervated heart (26). The foregoing evidence seems to be sufficient to show clearly that the adrenalin is increased in outflow into the blood and carried to the general circulation in consequence of emotional excitement.

Gley's failure to detect adrenalin either in the blood of the vena cava above the hepatic vein or in the blood of the heart, taken after splanchnic stimulation, and tested by a rise of blood pressure on being injected into a second dog, was, perhaps, as pointed out by Cannon (15, p. 428), due to the too small amount of adrenalin being doubly diluted. Tournade and Chabrol's recent experiments seem quite capable of settling this problem. Venous anastomosis was made in one instance between the jugular of one dog (A) and the right adrenal vein of another dog (B), and in another instance between the adrenal vein of one (B^1), and the superior vena cava

of the other dog (A^1). On stimulating the splanchnic nerves of one dog (B or B^1) whose suprarenal vein was operated upon, all signs of adrenalemia—a rise of blood pressure, increase of blood sugar, and dilatation of pupils—occurred in both animals. The blood taken from the animal in the height of adrenalin action caused no rise of blood pressure in the third dog when injected intravenously. These experiments obviously show that:

(1) The splanchnic stimulation brings forth the above phenomena in two ways, *i.e.*, by activating the adrenalin output and by nerve impulses, for the donor in these experiments has received no adrenalin in its own blood stream; and (2) the small amount of adrenalin is inactive when diluted into the blood of the body (**101, 103**).

In addition to all the direct evidence for the stimulating effect of emotional excitement on the adrenal activity, some indirect but important evidence is reported. That injection of the suprarenal extract produces in animals glycosuria was first found by Blum (**3**, ii, p. 246). Soon after this, Herter confirmed the fact with adrenalin. MacLeod has shown that the splanchnic stimulation will cause glycosuria, but will not do this if the suprarenals have been removed (**3**, i, p. 169). A number of clinical reports suggested that emotion would give rise to or facilitate the glycosuria, so-called "emotional glycosuria" (**14**, p. 67–68).

These observations are ample to infer that the glycosuria may be produced by adrenalin increased as the result of emotional disturbance. This inference was put to test by Cannon, Shohl, and Wright. Cats were used as the experimental animals. On being bound gently to the holder, some animals became so excited that "Young males usually became quite frantic, and with eyes wide, pupils dilated, pulse accelerated, hairs of the tail more or less erect, they struggled, snarling and growling, to free themselves" (**14**, p. 71). In all cats used (12 in number) including both excited and calm, "a well-marked glycosuria was developed" by means of binding, whereas before the experiment and one day after it no sugar was found in their urine. The time needed for developing the effect was paralleled by the emotional state of the animals. In those which showed signs of excitement early, sugar was found much earlier than in animals which subjected themselves to treatment more calmly. Thus the length of time of sugar appearing varied from 30 m. to 5 h. Further assurance that emotion can be the sole cause was obtained from this, that three cats, in which no sugar had been secured by mere confinement

for many hours, now developed glycosuria after being much excited for 30 m. by a barking dog that jumped at them from outside the wire cage in which each cat was put. Similar instances in regard to various laboratory animals were quoted by Cannon (14, pp. 74, 75).

Emotional glycosuria holds equally true of human subjects. It is too well known to be stated here that Cannon, Fiske, Smillie and others found glycosuria in the Harvard football squad and students who underwent a hard examination (14, pp. 75, 76). The great European war offered many similar instances where the glycosuria was associated with the great emotional stress, such as in case of aviators after a flight, and citizens after being subjected to the perils and excitement of bombardment (16, p. 27). Clinicians have long observed the emotional glycosuria elicited by emotional conditions. This is especially obvious in cases of diabetes. An interesting case is given by Pottenger. A diabetic who had become sugar-free "was playing croquet when a ball bounced and struck him on the chin. He was frightened and suffered some pain, and immediately had a return of sugar" (3, i, p. 168). In contrast with the foregoing cases is the well known fact that sugar is rarely found in the urine of patients or animals which have undergone severe operation or treatment during anesthesia.

That not only exciting emotion but depressive affection also may give rise to the condition of glycosuria seems to be true from the cases of students under hard examination as above referred to. But sugar in the urine, as pointed out by Cannon, is only a coarse indicator of the increment of sugar into the blood, and does not show the fine variations which the examination of the blood itself does. The most extensive study of glycemia of patients suffering from depressive melancholia was recently reported by Kooy (59). According to him, in melancholia the glycemia is much higher before meals, and in great excess shortly after a meal, disappearing more slowly than in normal individuals.

	Before breakfast, per mil.	¾ hr. after breakfast, per mil.	1½ hrs. after breakfast, per mil.	2¼ hrs. after breakfast, per mil.
Normal	0.98	1.14	1.16	1.04
Melancholics	1.13	1.63	1.45	1.19

The above evidence, both the laboratory experiments and clinical reports, agree altogether in one point, that emotional disturbances of any nature, exciting or depressive, may result in glycemia. Thus

Watson devises a new method for detecting the emotional effect of a stimulus making use of the blood sugar test (13, p. 220). It is certainly "unquestionably a very delicate indicator and revealer of emotional changes." But our concern is to see the adrenalin action in the mechanism of increasing the blood sugar content as the result of emotional disturbance. This is really a difficult matter, and there is much dispute among authorities (14, p. 77).

Cannon and his co-workers came to the conclusion that "the adrenal glands perform an important contributory rôle in the glycosuria." This was based on their experiment in which three cats, which had given quick glycosuria before, showed no trace of sugar in the urine after adrenalectomy, though the degree of excitement manifested was unchanged before and after the removal (14, pp. 77–78).

A good many observers, on the other hand, found that after removal of the glands glychemia or glycosuria could be produced. Among them Stewart and Rogoff appear to be the representatives, for their works have taken into consideration the available data on both sides, and apparently under the most careful conditions. Stewart's statement is as follows:

> "Whatever the mechanism of their [experimental hyperglycemia] production may be, the suprarenal bodies are not essentially concerned. . . . There is no evidence that 'emotional hyperglycemia,' if it exists, is at all related to the epinephrin discharge from the suprarenals. The possibility may be admitted that different species of animals, perhaps different individuals of the same species, may vary in their susceptibility to emotional excitement as regards changes in the blood sugar content. If this were so, man might be expected to be more susceptible than lower animals. Cannon, Shohl and Wright saw glycosuria regularly in cats as a result of emotional excitement, and Cannon found it in some of the students of a class subjected to the stress of an examination, and in football players" (3, ii, p. 160).

Obviously he denies the adrenals as an important factor in the glycemia mechanism, although he tends to recognize the existence of the emotional glycemia. No possible cause, however, is proposed.

However, negative evidence as a rule, including Stewart and Rogoff's, is adduced with the other conditions, as asphyxia, anesthesia, or piqûre, rather than the emotional states, and if the glycemia or glycosuria associated with the latter situation is to be fundamentally distinctive from that induced by others, as Stewart and

Rogoff claimed (3, ii, 160), this negative evidence is not only indirect but also entirely irrelevant to the emotional glycemia.

On the contrary, a considerable amount of positive evidence, direct and indirect, is brought out by many reliable investigators, including Cannon. Elliott has seen the lessening of the residual adrenalin content in the cats a day or so after they were admitted in the laboratory. They were described as "sulky, ready to snarl at their comrades, and very suspicious of their surroundings" (36, p. 379). Lewis' unpublished results, referred to by Watson (113, p. 220), conclusively showed in animals "that if the adrenal glands are removed emotional stimuli will not cause this increase in sugar either in the blood or in the urine."

Besides the direct evidence, there has been brought forth copious indirect testimony that injection of adrenalin produces glycemia, and removal of the glands prevents the occurrence of the phenomenon applying the possible stimuli (3, ii, pp. 247–249). Recently Carrasco added one support of this nature by a new method utilizing the denervated heart as an indicator of epinephrin. And he found that piqûre increased the heart-rate and that adrenalin also increases in consequence of piqûre (28).

It may be safely stated, therefore, that adrenalin is one of the important factors, if not the sole cause (100) in the production of glycemia in any case, including the emotional glycemia.

Returning to the original problem, another indirect support for the emotional output of adrenal secretion was brought out by Cannon and Mendenhall. After showing that the clotting of the blood is hastened by excitation of the splanchnic nerves, when the adrenal glands are intact, they found that the blood taken from the excited cats showed marked less length of coagulation time as compared with the calm animals. The cutting of the splanchnic nerves abolished the shortened effect of the excited blood. Cannon's previous works show that intravenous injection of adrenalin hastens the clotting time. Considering this fact with the above observation, they came to the conclusion that emotion induces the faster clotting of the blood and that this was effected by increase of the adrenal discharge. Histological changes in adrenal glands as the result of strong fear is alleged by Crile to be the effect of characteristic exhaustion (29, p. 198).

B. *The Thyroid Glands*

"Unfortunately, the thyroid cannot be studied to advantage either functionally or histologically, for there is as yet no available test for

thyroid secretion in the blood as there is for adrenalin, and thyroid activity is not attended by striking histologic changes." During the last decade various forms of tests for thyroidal secretion were advanced by many investigators (3, i, pp. 259–280; 89, pp. 361–364) but unfortunately the above statement of Crile (29, p. 213) seems to be still true. The denervated heart that was first used as an indicator of adrenalin by Dr. Cannon, was utilized by him for testing the thyroid secretion, too, because the effect on the heart-rate of each gland has characteristic aspects. By using this he and his collaborator obtained a remarkable result of thyroid secretion in consequence of afferent stimulation (24). If we think of the fact that this stimulation and emotion are always found by Cannon to have the same effect as adrenalin augmentors—indeed in a case afferent stimulation was treated as the representative of these adrenalin stimulations (21, p. 309)—we are not far from being justified when we take the above experiment as an indirect proof of emotional secretion of the thyroid. But this is no more than a mere analogy, and despite Cannon, assuming the probability of thyroid extra-activity in times of emotion, left the determination to future researches, no direct study is yet reported by him (20, p. 78). By using the method of the denervated heart it is highly desirable that the direct test for the emotional effect on the gland be furnished.

It is stated by Crile, a distinguished student of the thyroid, that the function of the gland is best evidenced by its rôle in the production of fever. Using this function he gives a more or less direct proof that "normal rabbits subjected to fear showed a rise in temperature of from one to three degrees, while two rabbits whose thyroids had been previously removed and who had then been subjected to fright, showed much less febrile response" (29, p. 217). From lack of detailed description it is impossible to know what was the stimulus used to make the animals fear, and to what extent they responded. And, if we trust him about the mental and physical conditions of the experimental animals, there is another questionable point, *i.e.*, whether fever is specific, and therefore, reliable enough as an indicator of the internal secretion of the thyroid. At any rate, however, it may serve as supporting evidence for the increase of thyroid secreted by emotion as the experiment was carried out by so competent an investigator.

If we are permitted to use theoretical speculation, it is very probable that the thyroid is called into extra activity in affective disturb-

ance, because (1) emotion is usually expressed along the sympathetic regions, and the thyroid is innervated and capable of being stimulated by the sympathetic fibers; (2) adrenalin stimulates the sympathetic activity in general, and, further, activates the thyroid secretion, as demonstrated by Cannon (20). Emotion, on the other hand, is proved to act on the adrenals increasing their internal secretion. These two possible relations may render the conjecture reasonable that there exists somewhat direct and indirect connecting channels of activity between emotion and the thyroid.

Direct experimental evidence is very meager, as seen above. Another mode of substantiation is clinical observation. Apparently Crile concedes too much to his own theory when he says: "Fortunately a vast number of clinical observations show a direct relation between the thyroid gland and the emotions" (30, p. 140), for exact clinical observation is just as difficult as the laboratory observations and, indeed, the situation is more complicated, as will be seen.

The etiologic theories of the so-called hyperthyroidism are not uniform. Besides toxic and infectious theories, two main theories regarding the relation of the thyroid and nervous system are conflicting; the one is the thyrogenic, the other the neurogenic theory (3, i, pp. 309–314). Which is the cause and which is the effect seems to be quite impossible and unnecessary to determine, for the condition of the onset may be able to vary according to the vast number of factors concerning the disease—personal character, predispositions, chance circumstances, etc. Probably both the thyrogenic and neurogenic theory may be duly applied to individual cases with varying conditions, and neither alone may cover the general cases.

Hyperthyroidism, whatever the cause may be, is a disease of the thyroid gland, with the condition of hyperactivity or dysfunction. In exophthalmic goiter it is generally believed that there is increased thyroid substance in the patient's blood, although for lack of exact test how much is not known. "It is difficult," says Schäfer (89, p. 364) "not to believe that there is constantly a very small amount of thyroid secretion circulating in the blood, and that this amount is increased in exophthalmic goiter." The term exophthalmic goiter is used by the average investigator to indicate a most fully developed case of hyperthyroidism, and very often as a synonym for Graves' or Basedow's disease, although some, especially quite recently, propose the distinction between hyperthyroidism and Graves' disease and exophthalmic goiter.

Of course the nervous system is not identical with the mind, but no one can deny the close attachment or nexus, as Sherrington calls it, which exists between the two. So, roughly speaking, the neurogenous is psychogenous, if we take the meaning of the former in a general sense without putting special emphasis on a particular part of the nervous system.

Many European investigators have observed the "war diseases" which were occasioned by the last Great War and the psychical or nervous agitation was considered as the direct cause of these diseases which involve endocrine disorders. Of these there are the "war Basedowism" studied by Rothacker, Stoney and others; the "war Addisonism" mostly studied by Sergent and other French observers; the "war diabetes" observed by Von Noorden (**80**, p. 332). Rothacker has shown many cases of soldiers who manifested an acutely developing Graves' disease caused by nerve concussion and mental excitement from machine-gun fire and trench warfare. A rest of several months' duration resulted in inevitable recovery. He also described similar cases from civil life which showed as the result of mental and emotional excitement, not only a remarkable enlargement of the thyroid, but also typical Graves' disease of which pathological symptoms soon disappeared when the psychical causes were removed (**83**). From these instances and many others he seems to believe many cases of Graves' disease are of nervous origin. Pende, a well known Italian neurologist, appears to advocate the same theory. But he thinks the neurogenic endocrine disorders are more incomplete, mild, temporary, and easily curable than the endocrinogenic (**80**, p. 332). Stoddard observed exophthalmos and a swollen thyroid in numbers of people during the German air raid on London, and he believes in the psychical origin of exophthalmic goiter (**97**, p. 375). Marañon, according to Cannon, has collected a large series of similar cases and has attributed the cause of them to emotion (**16**, p. 28). Gowers is referred to by Howard as stating that many cases of exophthalmic goiter occurred in Alsace and Lorraine during the Franco-German War of 1870 (**3**, i, p. 307). The same idea was apparently possessed by Rothacker, for he seems to see the primary cause of Graves' disease in the mental strain or emotional excitement, while the thyroid is secondary. Although in quite different thyroidal substances, qualitatively and quantitatively, from those usually alleged, Janney attempts to find the accountable toxic material of

Graves' disease; he also claims the psychic elements as the stimulators of these substances (55, p. 809).

The great excess of female cases of exophthalmic goiter over the male may have some significance in this connection. The ratio between the sexes is differently reported. Mackenzie has stated the proportion from statistics of cases in England and Wales during the four years (1911–14) as 10 females to one male (66), while in the United States 5.6 to 1 is reported from the Mayo clinic. The latter is approved as approximately correct by Howard (3, i, p. 306). The predominance of emotional life, and greater susceptibility to stimulation likely to cause affective disturbance, of the female, must be factors of great importance to be taken into account for the explanation of the phenomenon in question. If it were so, this is one of the indirect proofs of the fact we are trying to establish.

From the foregoing review of the clinical observations it may be justifiable to say that emotion will cause the hyper-secretion of the thyroid just as well as of the suprarenal glands.

We can hardly leave the discussion of the emotional influence on the thyroid without considering the affective psychoses in relation to the thyroid gland. Parhon showed that the average weight of the thyroid of insane people is largest in the affective psychoses—*i.e.*, mania, melancholia, mania depressiva—and least in epilepsy. Kojima, as a result of extensive post-mortem study of 110 cases of insanity, found no definite relation between the thyroid weight and the affective psychoses in the male, whereas in many female cases of affective psychoses he found a very large thyroid (57, pp. 36–37).

Regarding the histological changes of the gland in dementia precox, the results of various investigators are not uniform; *i.e.*, some show an alteration of hyperfunction, while others show sclerosis connected with hypofunction (8, pp. 400–401; 57, p. 89). Kojima observed a tendency to hypofunction in the male and to hyperfunction in the female (58). The number of his cases is rather small; but here again, as in his other study above referred to, we can see the preponderance of the female in hyperthyroidism.

Borberg seems to be sceptical of endocrine function in connection with mental disorder. To quote his words: "It is probable that the endocrine changes in etiological and pathological relation to every case as a part of psychoses may play a rôle. But in our present psychopathological classification no anatomical parallel can be drawn (8, p. 461)."

Recently, however, Witte has succeeded, more or less, in throwing light on the problem of the anatomical relation between the thyroid and dementia precox. As the results of study of 815 cases of dementia precox from the Institute of Bedrug, he found that in dementia precox (schizophrenia) the number of the cases of thyroid atrophy was remarkably small as compared with other forms of insanity (epilepsy, paralysis, etc.), and with mentally sound people. The influence of somatic diseases, like tuberculosis, heart disorder, and infections, very common in dementia precox, was studied by comparing the conditions of the glands of: (1) dementia precox patients with those of mentally sound people, both suffering from these diseases; and (2) the cases of dementia precox with those of other insanities, both free from these somatic diseases. In all cases the schizophrenic type showed a markedly low ratio in frequency of thyroid atrophy. "It may be well assumed," he stated, "that the relatively rare occurrence of thyroid atrophy is the fundamental of the disease of dementia precox, and of its bodily characteristics" (115, p. 195). We could cite abundant instances that illustrate thyroid hyperfunction in dementia precox, especially in affective psychoses.

The inference may be justified, then, that there is a close relationship between dementia precox in general and especially the affective psychoses and the thyroid hyperactivity—or at least infrequency of its atrophy. Now the question would be naturally raised: "Which is the cause, and which is the effect; the psychic process or the disease?" This is indeed a difficult problem. Unfortunately in our present knowledge no one, perhaps, can venture to offer any competent answer. Roughly speaking, however, there seem to be two tendencies among authorities, one looking for the cause of the disease in psychic, the other in organic disorder. The scope of the term dementia precox is too large and vague to make us hope to find its real and consistent cause in any definite factor or factors. Both psychical and organic origin can be duly assumed in dementia precox at large, or in a somewhat specific subdivision of the group as affective psychoses. Therefore, until a clearer division is provided and more definite etiology is advanced for each division we may have to be content with both of the causes now assigned, as alternatives having the same weight. If so, we may be justified in assuming that the tendency to thyroidal hyperfunction in dementia precox is caused, at least partially, by emotional conditions no matter whether exciting or

depressive in nature. With the cases of exophthalmic goiter during the war the inference of emotional origin is more reasonable. This may gain support from a study of Henderson who, by analyzing the precipitating causes of the anxiety psychoses of his cases, obtained the following results:

	Women	Men
Mental	37	23
Physical	14	4
Combined	14	5
	65	32

"Thus in 57 per cent women and 71 per cent men the etiological factors were mental, whereas physical factors were of importance only in 21 per cent women and 6 per cent men" (50, p. 278).

The death of near relatives, financial and business worries, unfortunate home conditions, the breaking up of the home, etc., are counted by him as the mental cause. Possibly the strongest and most abundant supporting instances of this theory are found in the books on psychoanalysis. Most recently Stoddart has expressed the view quite strongly, that the organic changes are secondary to the purely psychical disorders which are the primary and fundamental cause of dementia precox and of hyper- and hypo-thyroidism. This psychical cause is capable of modifying the endocrine secretions, and thus producing considerable organic changes (97, pp. 375, 378).

In concluding we should say that the theory that emotion stimulates the thyroid secretion to increased outflow, still lacks direct evidence, but, on the other hand, it can be proved fairly well by a good many indirect observations. Nevertheless, experiments of direct test are highly desirable.

C. *The Pituitary Body*

The pituitary body, as we have already mentioned above, is a complicated one, structurally and functionally. Moreover, the exact physiological activities of the hormone secreted from the different parts of the gland are not clearly established. Accordingly we have to be content with rather obscure evidence in any aspect of this organ; especially the experimental work attempted on the emotional influence on the gland has seldom carried on.

The only available record accessible to me is the one of Uno (105). His experiments were made with 41 pairs of albino rats. Two males from the same litter were put in a wire box, the wooden bottom of

which was studded with the blunt ends of nails. The nails were connected with the dry batteries through wires, thus the animals were stimulated for 4 seconds per minute throughout the experiment. By the electric stimulation and others such as pricking or pinching the tail, the animals were made to fight for 1, 3 and 6 hours. Some pairs fought severely, and were often clearly exhausted at the end of the experiments. Right after the experiments the animals' glands were dissected and compared with those of the controls from the same litter.

The results showed the following: (1) In the groups which were stimulated and fought for 3 or 6 hours, a slight average increase of the weight of the hypophysis was noted. But a difference in severity of the combat did not show any differentiation in the weight of the gland. On the other hand, deviation in the weight of the gland from that of the controls was greatest in the group of 3-hour fighting; in this group, again, the number of severe fights was also greatest. (2) The extract from the gland of the experimental animals showed the *contraction* of an isolated intestinal strip, adding a small amount (1.6 to 2.5 cc.; 25:10,000), whereas the extract from the control gland, prepared in the same manner, showed *relaxation* of the strip. This contraction occurred with the extract from all animals submitted to 1, 3 or 6 hours stimulation and fighting, or either electric stimulation or fighting alone; but did not appear from that of animals which had been subjected to less than one hour of either excitement.

Now of these results the first one probably does not deserve much attention, because increase of the weight of the glands in this case apparently shows little relation to excitement. The result with the group of 3 hours fighting, may be attributable to age, for that was the group of greatest maturity. The second result—modification of action of the extract—is promising. No explanation is given by the author. He only says, "stimulation or fighting changes the hypophysis so that the extract from the test hypophysis acts on the strip of the intestine like the glandular extract taken alone." This statement is made on the author's belief that the extract from the glandular part (anterior lobe) of the pituitary of the rat causes a marked contraction of the intestinal strip, while the extract from the nervous portion (posterior lobe) gives a relaxation. This belief, it is stated, is based on his own experiment which is supported by Degener's.

Shamoff, however, could not see any influence of the extract from the anterior lobe of sheep and oxen on the rabbit's intestine; while she did see marked *contraction*, after a transitory relaxation, induced by the posterior part of the same glands from which the anterior lobe extract was taken (**86**, pp. 276–277). Many experiments resulting in the same effects of the posterior lobe extract as those of Shamoff are cited by Hammet (**3**, i, p. 756). If this be true, the contracting effect seen in the test hypophysis in Uno's experiment must be ascribed to the posterior lobe instead of the anterior part.

What it may be, the different effect which Uno observed between the test and control hypophysis is unexplainable in our present stage of knowledge of the pituitary gland. Still, however, his experiment is interesting as well as suggestive in connection with our present problem; it would be more so if his procedure with the intestine and the degree of dilution of the extract added had been described more fully.

The clinical proof is very meager. For the active substance secreted from the anterior lobe of the gland, tethelin, is mostly concerned with the growth and development of the organism, especially the bony structure, thus the action of it is gradual; and pituitrin, the hormone from the posterior lobe, and, perhaps, from the pars intermedia, is not yet clearly known in its chemical nature. The effect of the latter, so far as it is known, is not specific enough to be judged from external diagnosis, being blurred by the action of the hormones from other endocrines—adrenalin and thyroid secretion—stimulated in common, as is ordinarily the case. "Only of late," writes Cushing, "with the development of roentgenology and the more extended use of the ophthalmoscope and perimeter can a diagnosis of pituitary disease apart from acromegaly be made with any probability. Unlike thyroid enlargement, a hypophyseal growth can be determined only by indirect methods; for next to the brain itself, the hypophysis lies in possibly the best protected and most inaccessible place in the body—one reason for assuming that it may be a most important member of the endocrine series." (**46**, pp. 57–58)

Frequently emotional disturbances are assigned as the preceding condition of acromegaly, according to Bassoe (**3**, i, p. 809), though this is confined to female cases. Pel is referred to by him as reporting three instances, so convincing that emotional shock should be accepted as an etiologic factor. If we think, however, of the fact

that the disease of acromegaly is quite rare and chronic in nature, and, on the contrary, that our emotional stress is so common, and usually transitory, we must admit that Pel's claim, which has no further support from other investigators, can not be accepted without doubt.

The matter is equally obscure in connection with the posterior lobe. Pituitrin, as above noted, is not yet purely isolated, and, it is said, probably has more than one component substance; for the effect of it oftentimes indicates quite opposite action on the same bodily structure and function. This causes much error and misinterpretation, not only in clinical but also in experimental investigations. Thus, naturally, conflicting conceptions prevail among students about the characteristic functioning of the drug. Polyuria, for example, is a popular clinical symptom coexisting with hyper- and hypopituitarism, and has been formerly considered as a result of hyper- (**88**, p. 113) or hypofunction (**31**) of the posterior lobe. If this be true, it is very promising evidence for assuming the emotional influence on the hypophysis. But from recent works (**3**, i, pp. 732, 879–880) its specific connection with the pituitary gland seems to be rendered unstable. The same destiny is menacing the glycosuria in which clinically, experimentally the posterior lobe has been alleged as playing at least one important part. Practically all possible clinical procedures are deprived of the promise of furnishing evidence of any kind for emotional influence on the pituitary body. This, of course, does not include the other clinical syndromes assigned to the hypophysis.

D. *The Liver and Pancreas*

There is no direct proof in literature that these glands may be directly affected by emotional conditions. Cannon's study to which we have referred above, showed that emotional excitement gives rise to glycosuria in animals, and numerous clinical observations have shown affective disturbance associated with glycosuria. The exact mechanism of the appearing of the glycosuria is in dispute. The liver, pancreas, adrenal, thyroid, and nervous system, and to some extent the pituitary body, are all considered more or less as playing certain rôles in sugar metabolism.

Many theories are proposed from various experiments. The effect of these endocrine glands, or even of the liver itself, on glycogenolysis, has sometimes proved slight. Pharmacodynamically

such hormones as adrenalin, thyroxin, pituitrin, are known as the stimulators of the glycogenolytic function; and on the other hand, most recently, since the discovery of the pancreatic hormone, insulin, the inhibiting effect of this drug has been eagerly studied by many, but the exact physiological mechanism is not yet fully determined.

In emotional glycosuria just how these organs partake we do not know. But if we admit that adrenalin performs an important rôle in this case; and that, as is usually thought, adrenalin acts on the glycogen content of the liver via the pancreatic hormone, these two endocrine organs, the liver and pancreas, become the sharers in emotional glycosuria.

According to many authors (Cannon *et al.*), adrenalin inhibits the pancreatic endocrine function which regulates the conversion of glycogen of the liver into glucose, and thus as the result of excessive increase of glucose in the blood the glycosuria ensues. If so, we may say that indirectly the internal secretion of the liver, if we may be allowed to call glucose an internal secretion, is increased, and, on the contrary, that of the pancreas is decreased or arrested by emotional stress. Theoretically this may be possible, if we follow one of the prevailing doctrines. Direct experiment, however, alone can give a clear explanation to this problem.

With regard to the other endocrine glands, we can state nothing about the influence of emotion upon them. From the study of physiologists, biochemists, and clinicians, the endocrine influence exerted upon the organism or on the central nervous system is relatively clarified. Unfortunately, however, the emotional effect on these glands has received very little attention, although it has equal significance. Indeed, in the normal condition the stimulation which activates and mobilizes our life is more dependent upon the psychical processes than on the bodily organs which are ordinarily called into activity by the former. Therefore, the study of this relation is, in some sense, more significant than the other.

2. Endocrine Influence on the Emotion

We have seen that emotional stress calls forth the endocrine outflow in increased amount. Now we are in a position to refer to the influence of the internal secretions on the emotional conditions. Indeed, the matter is of very great concern, because for completeness we have to describe the endocrine effect in its normal and altered states on emotion; and, further, the altered state in amount, in nature

for both increased and decreased cases. But this is almost impossible. A brief, incomplete description, which the available data would permit, would be the most within our power.

Injection of the active principle or the extract on the one hand, and the extirpation of the glands in question on the other, are the general experimental method. Implantation of the organs and the feeding of the glandular extracts are applicable methods for some glands.

Clinical and pathological observations also furnish important data. We shall present the apparently necessary data to the best of our ability without following any specific order.

A. *The Adrenal Body*

The locus where the adrenal secretion acts is generally believed to be the so-called myoneural junction, and not the central nerve cells, except in very few cases (3, ii, pp. 192–193; 252–255). Therefore if the nerve is severed from the central nervous system the effect of adrenalin is not interfered with, whereas, if the fiber termination is paralyzed no effect is seen, even if the tissue cell innervated by the fiber is irritable.

In this manner epinephrin acts on all the organs and tissues innervated by the sympathetic nerves and stimulates the activity of them; in other words, it stimulates the sympathetic action on the organism. Now it will be remembered that emotion expresses itself along the sympathetic realm activating the organs along that line, accelerating the heart rate, dilatating the pupil, etc. We have further seen that emotion calls forth the increased secretion of adrenalin. If emotion and adrenalin both elicit similar bodily reactions, and if emotion causes the adrenalin output, the questions naturally arise: first, what bearing has the epinephrin action on the emotional bodily changes; second, does it bring forth emotion itself or not?

A number of investigators noticed that the injection of adrenalin is capable of reproducing practically all the bodily signs which would accompany pronounced emotional conditions. None, however, described the adrenalin effect on the subjective emotional state so vividly as it is done by Marañón, an endocrine enthusiast in Madrid. When small amounts of adrenalin are injected into a human subject the general reactions are markedly yielded if the sympathetic system is sensitive. The blood-pressure rises, carbohydrate metabolism changes; localized tremor of hands occurs extending to the arms

and at times to the entire body; the face turns pale or becomes flushed, perspiration appears, at times tears flow, and mild polyuria ensues; the pulse rate increases, the mouth becomes dry, the pupils are dilated, the eyes become brilliant, and finally the sensations of respiratory and cardiac oppression are felt.

A sensitive subject, one with latent hyperthyroidism, gave the syndrome of terror without having been terrified, after receiving an injection of adrenalin. Oftentimes this circumstance was recognized by the subject himself who declared of his own volition "It seems as if I was afraid but I am calm." (Marañón, **68**) This artificial reproduction of the emotional bodily response without the subjective emotion is very interesting and important in view of the classical theory of Lange-James. Cannon has given a similar instance. "Some students at the Harvard Medical School, who had engaged in athletic matches, testified after receiving an injection of adrenalin, that they felt just as they had felt before starting a race—'all worked up and on edge.'" (**16**, p. 29)

The foregoing observations show that adrenalin well imitates the emotional syndrome and leads the subject almost to the edge of subjective emotion. The bodily conditions are present. All that is lacking of the usual emotional experience, is the psychic aspect. It is interesting to see whether a subject in this condition has any advantage for the real emotion. This has been observed by Marañón.

"One of the female clinical patients spoke of her absent children, of the dangers they ran without her care . . . but all without emotion. Ten minutes after the injection, of half a mgm. of adrenalin the same woman gave evidence of the physical signs of emotion induced by the drug, but all without psychic emotion; mention of her children, however, was sufficient immediately to arouse bitter weeping. This experience has been repeated in countless other cases with a distinct intensity according to the pathological and temperamental circumstances of the individuals.

"It appears as if adrenalin can produce all the emotional syndromes except the psychic factor. This factor alone is lacking to emotional expression, and when we complete it with an emotional memory, which previously was insufficient to produce an emotional reaction because of the lack of the sensitization by the somatic element, the emotion is produced in all its integrity." (**68**)

There is nothing to be added any more to the above regarding the adrenalin effect on the subjective side of emotion, which we look upon as the real emotion. One thing, however, must be kept in mind, *i.e.*, the foregoing statements, valuable and interesting as they

are, are of interest especially from the pharmacological standpoint. Their physiological value is another question.

Cannon has shown, by matching adrenalin injection with reflex adrenal secretion measured by the denervated heart-rate, that when the heart rate is accelerated between 30 and 42 beats per minute, the output from the adrenal glands lies between 0.0032 and 0.0037 mgm. adrenin per kilo per minute (27, p. 337). The increased beat of the denervated heart, when the animal was emotionally excited in his early experiment, was 38 per minute. The rate of adrenalin output estimated in a case of the reflex secretion seems to be applicable, therefore, to the emotional secretion too, if we regard the adrenalin liberation in both cases as eventually identical in mechanism and in nature, as Cannon believes. That adrenalin of this amount (0.0032 or 0.0037 mgm.) is enough to produce a rise of blood pressure has been shown in the animal test (3, ii, p. 198).

Unfortunately we are not informed what amount of epinephrin would be secreted in time of emotional stress in the human being; and from this lack we are unable to tell to what extent Marañón's experiment is applicable to the physiological activity of adrenalin secreted in the emotional storm. In other words, we cannot tell to what extent the amount of adrenalin used in his experiments is over or under the physiologically possible amount in our body at the time of the affective disturbance.

Neither is our information less obscure with respect to the clinical evidence whether there is any condition of hyperfunction of the glands of such a nature that the secreted hormone would exert its influence on the emotional condition. Indeed, frequently tumor of the adrenal cortex is associated with hyperfunction of this part of the suprarenals, and the resulting symptom of pubertas precox is ascribed to the oversecretion of the cortical hormone. If this be true, it furnishes a significant support to the view that the adrenal cortex plays an important rôle in connection with the development of the love emotion. Unfortunately this theory does not seem to have strong foundation. Recently Krabbe suggested a plausible hypothesis. In reviewing the cases of cortical tumor, in the literature, he found that in the case of girls the associated syndromes do not characterize the true precocious puberty; for in most of the instances ovulation and menstruation, the essential factors of the female pubertas precox, are lacking. It is not pubertas precox, but a virilism, according to Krabbe, that accompanies tumor in the cortex of girls. Acting on

the belief that in the embryonic stage the inner medullary portion of the ovary is testicular, he has tried to explain the virilism on the theory that the tumor of the adrenal cortex has not really been developed from ordinary adrenal cortex cells, but from the fetal testicular cells which have been absorbed by the adrenal cortex and developed as a sort of false cortex (60, pp. 4–8).

If this new theory is to be taken as true, as Krabbe has claimed, the pubertas precox with tumor of the adrenal cortex has no connection with the function of the cortical part of the gland, but with the testes. A supposed important function of the cortex—that it has close connection with the reproductive organs—is once again thrown into obscurity by this theory.

After all, our knowledge either of the medulla or of the cortex of the adrenals is in so chaotic a state that we don't know of any influence which they exert through their physiologic hyperactivity on the mental processes.

The question what rôle does hypofunction play in connection with the present problem is of significance rather abnormal or pathological, with which we have little concern. A brief review, however, is unavoidable since it aids in a better understandng of the normal mechanism. The effects of acute insufficiency are best demonstrated by surgical extirpation of the glands in question. The effect of adrenalectomy, especially that on the sympathetic system, was best shown in a report by Elliot, based on his experiments on cats during 12 years before that time. In a series of 25 cats the glands were removed in two operations, three weeks to nine months apart. Survival ranged from six to twenty-three days after the second gland was removed. In another series of 21 animals both glands were excised simultaneously, the animals dying usually the second day. The symptoms were very similar to both series. The weight progressively decreased, the characteristic asthenia developed, as in general, just before death. Yet no variation was detected in the emotional state. To quote his words, "Emotionally it showed no annoyance, and would purr in a languid way until near the final collapse." (39, p. 40)

Cannon's cats showed the same signs of excitement or rage before and after the adrenalectomy. "Indeed," he stated, "one was more excited after removal of the adrenals than before." (14, p. 78, see also p. 57)

Stewart is of the same opinion as Cannon on this point, although

he goes farther than Cannon denying even the significance of epinephrin as the maintainer of the sympathetic irritability (3, ii, p. 165). From the foregoing evidence it may be taken for granted that, whatever influences the adrenal secretion, including that of the cortex, may exert on the mental factors, they are not of such a nature that the sudden deprivation of the adrenals causes gross changes.

One more point remains to be considered. If acute insufficiency fails to show any appreciable change in the emotional life of the subject, does it not affect him in a chronic manner? Unfortunately no answer is possible. It is true that Addison's disease seems to have a close connection with hypoactivity of the adrenals, and general mental defects as well as emotional disorders are described among the symptoms of the disease; but until the certainty of this connection is more clearly established it may be wise not to take this as being a representative case of underactivity of the adrenal body.

"Addison's disease," writes Vincent, "is still the only well defined syndrome recognized as connected with the adrenal bodies. It is sad to have to admit that up to the present time it has not been possible to correlate in any certain manner any of the physiological observations on the glands with what we know of the symptoms of Addison's disease. It may be, after all, that disease of neighboring nervous structures plays a part in the production of the disease." (110, p. 317)

All experimental works, indeed, have failed to produce the most characteristic symptom of the disease, pigmentation, artificially; and all attempts at the relief or amelioration of the disease by the introduction of the adrenal extract so far has ended in negative results. On this point we are in the same obscure situation as we find ourselves in regard to the condition of hyperactivity of the gland. In concluding we may quote Vincent again: "It is too early to attempt to diagnose clinically any syndromata due to hyper- or hypo-function of the adrenal bodies." (108, p. 144)

Suggestions as to the importance of the adrenal cortex in connection with the central nervous system are provided from another angle of the study. Sir F. Mott, from the post-mortem study of the glands, found that the cortex of the adrenals shows great diminution in weight, thickness and lipoid content in dementia precox. Because of the great importance of lipoid substance for the general living cells, especially for the early development of the cerebral

hemispheres, he seems to be of an opinion that the cortical cells of the adrenal glands have an important connection with the central nervous system. For the support of his theory he pointed out the fact that there is a correspondence in size of the adrenal cortex and the brain development in the animal series and a great diminution in size of the adrenals in anencephalous monsters (**72**, p. 15; **75**, p. 700). Rossi of Madrid, referred to by Tucker, calls attention to suprarenal exhaustion and insufficiency in manic-depressive states and notes favorable results with suprarenal treatment (**104**, p. 262).

Indeed, a great effort has been made to find the endocrine connection with mental diseases; and as a result many important glands have been found in variations showing the possible relations, yet no definite correlation between the two is found, especially for the adrenal glands.

From the foregoing statements we may conclude concerning the adrenal influence on emotion, that in acute modes, for both over- and under-secretion, no direct influence can be demonstrated; whereas for chronic conditions the evidence is too meager to say anything decidedly.

B. *The Thyroid Gland*

Crile calls the thyroid "the organ of the emotions" (**30**, p. 141). Levy and Rothschild call it "the gland of the emotions" (**78**, p. 991). These investigators apparently call it so from their clinical observations. Truly clinical evidence is more tenable for this gland than for any of the others; and some symptoms of the disease in which the thyroid is involved easily impress one with the belief that it is "the gland of the emotions." Evidence, however, is not plentiful enough to warrant the immediate acceptance of this theory.

We have stated that the acting point of adrenalin is in the main the peripheral neurocellular junction. The location where the thyroid secretion acts is not so obvious. Whether it works directly on the organs, or its activity is mediated and effected through the nervous system is in dispute. Schäfer is one of the advocators of the view that the thyroid has a direct action on the cells of the central nervous system (**89**, pp. 357, 760).

Pharmacodynamic effects of the thyroid extract or thyroxin of Kendall are differently interpreted by sundry observers and the resulting symptoms are variously stated. Unlike those of adrenalin, they are brought forth with some delay of 24 to 36 hours; and both oral and intravenous introduction produce practically the same

symptoms. In regard to the mental and nervous phenomena in conjunction with the thyroid administration there seem to be few authenticated cases in which even a suggestion of this subject can be found. Schäfer, however, expressed quite clearly his favorite opinion as to the mental effect of the thyroid extract:

"If thyroid extract," he stated, "is administered to a normal individual—the dose varies with the activity of the extract and with the idiosyncrasy of the subject—signs of nervous excitation soon show themselves. There is a feeling of restlessness; the heart beats rapidly and often irregularly; the respirations are fast and shallow; the blood vessels are dilated; the skin is flushed and feels hot; the activity of the sweat-glands is increased; there may be diarrhea. With large doses the psychical excitement is accompanied by hallucinations, and may even simulate mania; there is sleeplessness; tremors of the limbs are common, and the reflexes tend to be exaggerated. In extreme cases there may be exophthalmos and dilated pupils. . . . On ceasing the administration, the symptoms which it has produced subside." (89, p. 357)

These effects he assumed are caused by the action of the thyroid substance or substances on the cells of the central nervous system. It might be supposed that these effects of the thyroid extract on the organs are caused in part by adrenalin, because of their great resemblance to the physical symptoms produced by that substance, and because of many evidences which have proved the adrenalin increase in the blood as the result of thyroid feeding. But according to Schäfer adrenalin plays little part in this connection; although as the consequence of excess of the thyroid substance all the cells—secreting or nervous—being rendered hypersensitive to the action of adrenalin, adrenalin may be responsible for some of the phenomena produced by the thyroid administration. He appears to come to this belief from the fact that with the blood from the exophthalmic patients no appreciable amounts of adrenalin can be tested, and that some of the cases of this disease can be treated successfully by the adrenalin administration (89, p. 369).

If this be true the thyroid substance is capable of producing such remarkable influence on the mental processes as "nervous excitation," "feeling of restlessness." Crile has noted a similar effect of iodine administration on the emotional state. "Excessive administration," he stated, "of iodine often causes a pathologic emotional state which cannot be distinguished from Graves' disease, and in continued overdosage, iodine may even cause Graves' disease." (30, p. 141)

Another group of investigators, however, claim that the thyroid extract never produces nervousness or any mental changes. Among these are Carlson, Rooks and McKie, who performed extensive experiments on various kinds of mammals and birds with thyroid feeding. In the results from the two experiments on man with daily feeding of desiccated sheep's thyroid the distinct effects were (1) loss of weight, and (2) dizziness and weakness, and (3) tachycardia. But "there was no evidence of nervousness, either subjective or objective" (27, p. 156). In one of the above cases the feeding continued 18 days with 1 to 2 gm. of thyroid daily; in the other case for 6 days with 2 gm. a day. Perhaps it might be supposed that the doses are too small to produce any mental effect, but on the last day of the second case 12 grams was fed in one dose and the condition was the same as it was previously. According to these investigators man has a relatively high susceptibility to thyroid administration per ounce, as compared to other mammals and birds, which they tested; and in the first case of the human subject the experiment had to be discontinued because of the subject's dizziness. Apparently susceptible as man is, it seems to be quite difficult to induce any effect on the mental processes.

In the series of experiments the above investigators noted that the carnivorous animals (dog, cat, fox) are more resistant to thyroid feeding than the omnivorous and the herbivorous; and considered that even in them the toxic effects produced are probably not due specifically to the thyroid, but are complicated by the effects of the excessive animal protein diet. If it be so, just what is the toxic agent in the thyroid substance is not fully known, the majority being inclined to attribute it to iodine (10). Whatever it may be, the pharmacodynamic effect is not after all the physiological effect. The latter has partially been shown by the noteworthy experiment carried on by Dr. Cannon, best described in his own words:

"It is a matter of interest to know if continued stimulation of the thyroid would have characteristic effects. This idea had been tested by connecting the central end of the cut phrenic nerve with the peripheral end of the cut cervical sympathetic trunk. This is a union of motor fibers with preganglionic fibers—a combination which Langley long ago proved capable of functioning. When the phrenic neurones grew out to the previous distribution of the destroyed cervical sympathetic axions, they would discharge into the innervated structures a volley of nerve impulses with every respiration. Thus the outlying neurones affecting the thyroid gland, in case the phrenic elements grow into contact with them, would be continuously excited

by normal impulses from the central nervous system. By this procedure we have been able in a certain percentage of cases to produce many of the phenomena of hyperthyroidism. The heart rate, which in the cats is approximately 150 beats per minute, increased to 225 and even to 250 beats per minute. The character of the animals changed from that of quiet, affectionate domestic pets to that of furtive creatures running away from anyone entering the room. There were loose movements of the bowels without evidence of fermentative changes. The most typical alteration, however, was a great increase in metabolism. Removal of the thyroid gland on the operated side in one of the animals restored the metabolic rate, which had been nearly doubled, to a level which was within the normal range of variation." (16, p. 24)

This is an experiment of great importance for many aspects of medical science. Artificial stimulation of the nerve may as a rule have many concomitant results which have no necessary relation with the nerve in question, on account of the surgical operation and of the inevitable involvement of other nerves in the stimulation. And the most unsatisfactory deficiency in the artificial stimulation is in the matter of time; for in an experiment of this nature the duration of the stimulation is limited to a rather short period, which probably might not be enough to compare with the physiological or pathological cases in ordinary life. Cannon's experiments above cited have been able to eliminate these defects to a great extent. So if we admit the results which were thus produced and the interpretation given by him as such, it shows quite obviously; first, that the thyroid is under the control of the cervical nerves; and second, and this is more important for our present purpose, that the thyroid substance thus secreted in an increased amount is responsible for changing the emotional character of the subject. Unfortunately this remarkable experiment suffers from lack of confirmation, many investigators having failed in getting similar results using supposedly the same procedure (107, p. 169).

From the foregoing brief review we may be justified in stating that in the realm of laboratory experimentation, pharmacologic and physiologic, two contradictory views are prevalent, favorable and unfavorable to the thyroidal influence on emotion, each view being supported by evidence of perhaps equal weight.

Clinical observations afford somewhat stronger evidence supporting the view that the thyroid can affect the mental activities. We have already often spoke of Graves' disease as if it were a representative case of hyperthyroidism. It has also been stated that both

the neurogenic and thyrogenic theories of the disease are plausible. Recently, however, an opinion has been advanced by Janney to the effect that Graves' disease is not caused by the hyperfunction of the thyroid, but by dysfunction (**55**).

Nevertheless, exophthalmic goiter, as we have already stated, is usually taken as an extreme case of Graves' disease or of hyperthyroidism. Let us hear Professor Schäfer:

"In exophthalmic goiter there is strong evidence that the thyroid is in a condition of superactivity. It is true that there is less colloid and probably less thyroxin in its vesicles, but this is what one might expect in an overactive gland, which would be pouring out its secretion into the blood as fast as it is formed—instead of storing it up in the alveoli, as one finds to be the case in endemic goiter." (**89**, p. 358)

If we take, and it may be safer, exophthalmic goiter or Graves' disease as hyperthyroidism, the first question to be taken up is, "What are the syndromes of the disease, especially those of its mental phase?"

Among other symptoms, Schäfer refers to the mental ones as follows: "There is nervous and psychical excitement and often muscular tremors. . . ." (**89**, p. 359) He attributes these phenomena to the direct action of the thyroid substance on cells of the central nervous system. The mental symptoms of exophthalmic goiter are probably best presented by C. P. Howard:

"Mental irritability, excitability and restlessness are among the early manifestations. The subjects long for continual changes and must constantly be seeing or doing something new. At times the patient is low spirited and tearful; at others cheerful and smiling but always resents being thwarted or contradicted. Apprehension and anxiety are especially common.

"The moral nature may be so perverted that the patient becomes spiteful, untruthful, suspicious and generally discontented. The intellectual powers may remain unimpaired, but various phobias and obsessions are also frequently noted. Some patients have a morbid exaltation with a capacity for great mental labor. This mental condition is aptly described by the term 'chorea of ideas.' In many cases these early symptoms are diagnosed as either neurasthenia or psychasthenia, and the underlying hyperthyroidism is overlooked. It is a good rule to consider in every case of neurasthenia or mild psychosis the possibility of an underlying hyperthyroidism.

"We are more in agreement with Parhon, Matéesco and Tupa, who consider that the psychic functions are influenced and regulated in a large measure by the activity of the thyroid gland. We would,

therefore, suggest that the mental excitement and unrest at least—possibly even the actual psychosis—may be due directly to the hyperthyroidism." (**3**, i, pp. 346–347)

From the above quotation it is clear that in hyperthyroidism mental changes of various aspects are common.

In regard to the thyroid relation to the mental disorders, however, the situation is not so clear that we can accept the suggestion of Howard without comment. Evidences are equally strong for both denial and recognition of the close connection between the thyroid and insanity. Some found hypertrophies, while others observed atrophies of the gland in the same type of mental disturbances. Mott has shown the hypothyroidic picture from the post-mortem study of a manic-depressive condition (**73**, pp. 59–60) and the same is reported recently by Parhon (**40**, b, p. 215). On the other hand Kappenburg has seen manic-depressive insanity or melancholia among goitrous patients (**3**, p. 347). A similar contradiction has been met for the other types of insanity. Probably it is too early to say anything conclusively about the correlation which possibly exists between the endocrine glands and mental disorders.

Perhaps none of the other endocrine glands can exceed in their clear-cut effects on the mentality the thyroid gland when it is in a condition of hypofunction. This has been a very well-known fact for a long time and consequently a brief, general account will be sufficient.

The complete surgical removal of the gland is inevitably followed by cretinism in children and myxoedema in adults. Transplantation of the gland—usually the graft is absorbed and decays before long—or the administration of the endocrine extract makes up the deficiency produced by the loss or defect of the gland, at least to so great an extent as to approximate the normal. After citing in detail the symptoms of cretinism given by Falta, Harrow says: "If now there still remains some question as to the soundness of the diagnosis, all doubts are immediately removed by prescribing extracts of the thyroid gland to the young sufferer. The recovery as a consequence is little short of miraculous" (**46**, p. 19). He probably stated this overemphatically to secure a better hearing. Nevertheless an agreement is reached among the endocrine students that the thyroid therapy almost inevitably brings about at least some temporary improvement of the mental condition of the thyroid defectives, though the effect is less prominent than that on the physical side.

Mott has found the degenerative changes in the nerve cells central and peripheral, in the hypothyroidal patients dying in the asylum (74, p. 52).

Clinical mental pictures of hypothyroidism, cretinism or myxoedema, involves the deficiency of practically the whole mental activity. In the young when the brain development is arrested, idiocy may be complete in the severest case. Mental backwardness may attract the attention of parents or teachers. Dullness, general apathy, sluggishness are apparent. The psychic condition of the cretin is classically described as heavy and listless. In severe cases mental depression is followed by melancholia in older hypothyroid patients. Such are the most frequent type of thyroid defective children, yet another type in certain cases is reported as characterized by nervousness, crying and screaming on slight provocation. Numerous clinical cases are to be found in detail in a monograph by D. W. Fay (41).

Sexual psyche is generally said to be retarded in development with consequent tardiness in appearance of puberty. In serious cases the libido may be entirely lacking.

The relation of hypothyroidism to insanity is not satisfactorily clear. A number of investigations, however, have been reported in the literature. Of 110 cases of post-mortem study of insane subjects Kojima found that the average weight of the thyroid in both male and female is extremely low, as compared with the minimum weight in other than mental cases given by other investigators. In his cases the average weight of the gland in 50 males was 16.46 gm., and in the 60 females 16.87 gm.; while the normal minimum weight by other authors, referred to by him, was 22 to 25 gm. In 12 per cent of males, and in 18 per cent of females of his own cases the thyroid weighed less than 10 gm. (57, p. 22). But it is noteworthy, as we have already noted above, that in many female cases of affective psychosis it was very large (57, p. 37).

Mott seems to believe a manic-depressive condition, associated with mental confusion, hallucination, delusions, "may arise as a result of a particular form of hypothyroidism with the increase of colloid in the pars intermedia of the pituitary body" (73, p. 59). Many investigators have found the thyroid lesion in various types of insanity. Among them the most recent, Lewis, observed histological changes in the endocrine organs of many cases of dementia precox, indicating deficient function; and he believes this is a part of the

underlying cause of insanity (**63**). Rutherford puts special stress on hypothyroidism, expressing his strong confidence that inheritance of insanity is of purely hypothyroidal nature (**84**).

H. A. Haynes of the Michigan Institution for the Feebleminded, found that at least one-fifth of the 1,200 cases of feeblemindedness examined gave evidence of disorders of endocrine function, a majority of the cases being due either to hypothyroidism or hypopituitarism (77).

In concluding we may say that for the thyroidal influence upon mental activity and emotion the positive evidence is not satisfactorily advanced; that the negative evidence is more outstanding, the resulting changes in mental status after the thyroidectomy or the extract injection in the defective patients are remarkable. It is desirable to know to what extent the general metabolic variation influences the changes. For the thyroidal effect is most profound on the metabolic rate. More clearcut experiments are needed, however.

C. *The Pituitary Body*

So far no record is available as to the direct pituitary effect on the emotional conditions. The secretion from the anterior lobe chiefly concerns the body growth of the organism, while that from the posterior lobe and probably from the pars intermedia acts very likely as the hormone of the suprarenal and thyroid, this oftentimes is grouped in the same class. Schäfer has shown three actions of pituitrin on the blood vessels different from that of adrenalin (**88**, pp. 44–46), which, however, need not be quoted here. According to him, aside from these three different actions, pituitrin does not specifically stimulate structures innervated by the sympathetic as does adrenalin. Probably it acts, he says, as a direct stimulus upon the contractile substance of the cells which it influences (**88**, p. 88).

This mode of action of pituitrin on the organs—direct and not through the nervous fibers—would presumably account for the fact that no report on the results of pituitary feeding has given any appreciable evidence regarding its effect on the nervous system. Muscular tremors are referred to by Dean Lewis (3, i, p. 728) as a nervous manifestation resulting from pituitary extract fed in large doses to young rats. He attributes this effect to the posterior lobe element. This is the only reference so far as I am informed as to the effect of pituitrin on the neuromuscular system; but far from a psychic effect.

The effect of the feeding of anterior lobe on the sexual develop-

ment, reported by Goetsch (3, pp. 729–730) is somewhat promising for our present study. It is true that this promoting effect on sexual development in the animal (rat) only shows the indirect action of the pituitary as it is being brought about as the result of premature development of the internal sexual organs, which, in turn, are stimulated by the hormone; yet it is certainly remarkable that this indirect relation has shown itself in shortening the period of complete sexual development by about one-third of its normal time after only 40 days of feeding.

After a brief review of the hypophysectomies performed by Cushing and by Achner, Lewis summed up the results as follows:

"Experimental removal of the entire hypophysis indicates that the organ is essential to life. Removal of the anterior lobe is the equivalent of total hypophysectomy. The anterior lobe therefore forms the secretion which is indispensable.

"Partial removal or destruction of the anterior lobe in young animals is followed by a peculiar train of symptoms—taking on of fat, genital atrophy, falling of the hair, temporary polyuria and glycosuria, and skeletal changes, which is quite comparable to the changes of dystrophia adiposogenitalis or Fröhlich's syndrome as observed in man.

"Removal of the posterior lobe, in which is included the greater part of the pars intermedia—has no early or late results. . . .

"It has been suggested that many of the changes associated with dystrophia adiposogenitalis are due to interference with or alteration of posterior lobe secretion—which means pars intermedia secretion. There seems to be no experimental evidence to support this claim." (3, i, p. 724.)

This last mentioned opinion, contrary to that hitherto generally accepted, is advocated by many authoritative endocrine students such as Hoskins and Vincent (51, p. 623), (110, p. 318).

The recent work done by Camus and Roussy and by others showed that many of the syndromes usually attributed to the pituitary lesion are really due to damage to the region of the third ventricle. Biedl, however, seems to recognize the pars intermedia as well as the base of the brain as the cause (7).

Cushing describes the results of hypophysectomy in lower animals as adiposis, hypersomnia and sexual dystrophy for adult animals; and the persistent infantile aspect and behavior for those deprived of the gland early in life. These conditions, he says, are those found in human beings afflicted with a corresponding secretory insufficiency due to tumor, anomaly or disease (31, p. 975).

The real cause of acromegaly and giantism is by no means more

clear than that of dystrophia adiposogenitalis. For it has no support from the experimental work in which all attempts to produce the same condition as these diseases by pituitary feeding have not given satisfactory results. At present, however, it is generally believed that these morbid conditions are caused primarily by glandular hyperplasia and functional overactivity of the hypophysis, especially or chiefly of the anterior lobe. The following summary as to pituitary disease given by Tidy gives us clearly the present view:

> Anterior lobe: Overaction, giantism before union of epiphysis; after, acromegaly. Underaction, before puberty, Loraian type of infantilism; after puberty condition unrecognized.
>
> Posterior lobe: Overaction, condition not recognized. Underaction, diabetes insipidus.
>
> Whole gland: Underactivity leads to dystrophia adiposogenitalis, adiposity, genital dystrophy, and infantilism varying in type according to its commencement (before, during, or after puberty). (98, p. 602)

Now we are in a position to see the mental condition in the disease caused by the pituitary disorders with the purpose of appreciating the relationship we are considering. The mental status of adolescent psychoses due to pituitary dysfunction is best described in summarized form by Tucker, a distinguished student, as follows:

> Group 1. Preadolescent hypersecretion with further increased secretion during adolescence. Mental symptoms consist of prejudices and infatuations, increased libido, psychomotor acceleration, transient hallucinations and sudden changes in temperament. These cases are usually diagnosed as hysteria.
>
> Group 2. Preadolescent oversecretion with decreased secretion during adolescence. Mental symptoms consist of indifference, drowsiness and at times trance states.
>
> Group 3. (a) Preadolescent normal secretion with an increase of secretion during adolescence. Mental changes slight, showing overfondness for dress and attention, somewhat increased libido and general nervousness.
>
> (b) Preadolescent normal secretion with a decrease of secretion during adolescence. Mental symptoms consist of dullness, seclusiveness, repetition of movements, inability to express, and irritability; they may or may not have hallucinations. The condition resembles dementia precox (104, p. 261).

Apparently the oversecretion induces abnormally accelerated men-

tal activity, and the undersecretion brings forth the reverse conditions in the case of adolescent psychoses.

This, however, does not seem to be a wholly applicable symptom. For many of the reports characterize the mental conditions of acromegaly with these words, dull, lethargic, indifferent, depressive; or apathy, lassitude, drowsiness, etc., although, according to Cushing, outstanding mental aberrations are rather rare. Only three of the 30 or 40 acromegalies in the series of his cases showed clear mental derangement. All three were hypersensitive women in an acute stage of the disease, and one of them showed a well marked manic-depressive syndrome with ultimate suicide. Truly he regards the syndromes above mentioned as the effect of hypersecretion on the mental processes, and not, as some do, the effect of hypofunction which usually follows acromegalic malady, but he acknowledges the fact that hypopituitarism is accompanied more often by drowsiness and indifference (31, pp. 972-975). Emotional derangement is milder or slighter in hyperpituitarism patients than in defective cases. The latter are sometimes referred to as emotionless and affectionless.

It is worth while to note briefly in this connection the relationship between the pituitary gland and the sexual desire, though it is indirect. We have already referred to the fact that hypophyseal insufficiency is always accompanied by sexual inactivity in structure and function. Goetsch's feeding experiment, above referred to, has further shown that prolonged feeding of anterior lobe extract, 8-9 months, called forth the early awakening of the sexual instincts, along with the premature growth of the sex glands. The breeding activity was more vigorous in every respect in the fed rats than in the control. L. N. Clark's feeding test on chickens is often quoted. After feeding of the pituitary extract for five days the egg production of 35 hens was raised from an average of 18 per diem to 33; at the same time the fertility of the eggs and hatching out of the chicks was extraordinarily enhanced. Apparently the pituitary secretion was in a state of close relationship with the generative glands. Cushing's inference, in view of the fact that the secretory discharges from the pituitary may be elicited from the sympathetic nervous system, that the liberation of the pituitary hormone may account for the recognized effect of the emotions upon the sexual sphere (31, p. 988) is highly suggestive, though we cannot help feeling his overemphasis on this gland.

D. *The Gonads*

(1) The Hypofunction and its effect.

From time immemorial a close connection between sexual gland and emotional life has been practically well known. That castration of the male animal is followed by a great change of the emotional status of the subject is common knowledge; and this has been practised since antiquity for practical purposes. Our present information on this point, unfortunately, is not far beyond the common knowledge.

The physical changes which ensue after castration in both sexes are very remarkable. In lower animals in which the secondary sexual characters are so different between male and female, the effect of castration is seen most strikingly (**69**, p. 305ff). The male will lose its outstanding token of maleness, such as antlers in the stag, comb and spurs in the cock. If the castration is performed in early life before the secondary characters develop, most of them, if not all, will never appear. Injection of the extract from the testis, on the other hand, arrests the effects of castration and restores the normal sexual appearance (**69**, pp. 309–310).

It is noteworthy, however, that the condition is remarkably different in the case of the female. The female animal which has its ovary spayed, not only loses its own secondary sexual characters, but male characters make their appearance.

A transplantation of the testicle or the ovary has been performed by many; the effect described has been that the graft, when it is "taken" successfully, acts just like the normal glands, even when it is planted in an abnormal position, as in the kidney or the abdominal wall; hence the function of the gonads as endocrine glands is made obvious. The graft will function (at least for the time before it shrinks) to restore the secondary characters in both sexes or will arrest the development of the opposite sexual characters in the female after the castration.

Recently Lipschütz and his co-workers studied the effect of castration in guinea pigs and found that if one per cent of total testicular substance is left the normal somatic sexual characters will be preserved (**64**).

From the above statements it is obvious that the somatic secondary characters are dependent upon the endocrine function of the sex glands both in male and female. Now we have to see the gonadal effects on the mental condition.

As might be expected, the closest relation of the generative glands to the mental sphere is made most apparent in the sexual desire. And in the lower animals this desire is most vigorously disclosed in the time of heat or mating season.

A number of experiments are cited by Marshall in which heat disappeared after ovariotomy, and was regained by transplantation of the ovary, in various kinds of animals. Among those he has given an instance of his own experiment collaborated by Jolly, which, because of its deviation from the ordinary one, must be cited. The fresh ovarian extract obtained from femals dogs "on heat" was injected into the other bitch the ovary of which had been previously removed. The anoestrous animal as the result of receiving the injection showed a transient congestion of the external generative organs resembling that of the normal proöestrous condition (69, p. 334).

Veterinarians are, it is said, generally agreed that heat does not occur in dogs whose ovaries have been extirpated. Sometimes ovariotomy is practised on mares in order to prevent heat, and consequently to suppress the undesirable symptoms which are liable to render the animals periodically unworkable. For the same purpose, it is very well known, the testicles are usually removed from a stallion.

In cold-blooded animals there is a periodicity in appearance of peculiar somatic changes. Nussbaum's much quoted experiment is of extreme interest in this connection. He found that male frogs from which both testicles have been removed before the copulation period not only do not develop the swelling of the thumb and other somatic changes essential for the prolonged sexual embrace, but show no tendency to seek the female. He has further testified that transplantation of a piece of testis from another frog will restore the normal sexual characters (89, p. 352).

Furthermore, according to Schäfer, the injection of testicular substance from mature frogs causes the embrace-reflex to become possible in castrated frogs, and this substance exists in the testicle only during the spawning period, and disappears after spawning is finished (89, p. 352). This is highly suggestive. There is no available record regarding the seasonal change in amount of the gonadal secretion for other animals; but, if we are permitted to infer from the above fact that gonads are in a condition of hypersecretion in the sexual season, it would afford additional significance to the gonadal function in relation to the phenomenon of heat. Perhaps

we should go too far beyond the fact if we assumed that we can account for the mental modification usually associated with menstruation in the human female by the same inference.

So far our description has been confined to the lower animals. As it might be expected the present problem is not so clear with respect to the human being. There is, however, a vast accumulation of records as to the results of removal of the gonads.

Castration causes nearly similar effects in man as in animals. The marked masculine characteristics, such as strong skeleton, low voice, beard, etc., are displaced by those of somewhat feminine type. Even the positive feminine signs, such as large pelvis, abundant hair on head and scanty hair in abdomen, etc., are often, not always, observable. When the castration has taken place in early life, the development of the whole genital tract is interfered with.

The sexual desire, it is said, may be extinguished, or it may continue in greater or less degree, the former probably being the case with the early castration. The following case reported by Lespinasse is of great interest for not only the problem at hand but also for many other reasons.

"A man, aged 38, consulted me in January, 1911, to determine if anything could be done for him to compensate for the loss of both testicles. . . . He was unable to have intercourse, which was his chief reason for coming to me. . . .

"On the fourth day after operation (a testicle from a normal man was transplanted in a normal position), the patient had a strong erection accompanied by marked sexual desire. He insisted on leaving the hospital to satisfy this desire. The desire and power of erection continued for five years, since which time I have lost track of him." (3, ii, p. 516)

Lespinasse believes that the sexual libido of eunuchs as a rule is below normal, though the general mental attitude varies greatly.

The general mental characteristics of eunuchs is available in the report of Hikmet and Regnault on the eunuchs of Constantinople, cited by Marshall (69, p. 305, footnote)

"They are avaricious, illogical, obstinate (*i.e.*, cannot change their idea), have no judgment, accept information without proof; are cruel, but fond of children and animals; are faithful in their affections, but have no courage; their mental activity is very slight, and they are extremely fanatical."

Apparently their mental picture is more akin to that of women than of usual normal men.

With regard to the effects resulting from ovariotomy in the human subject, our information is very meager, especially little is known of the case of early extirpation. The only reference in the literature to the effects of early castration in the human female seems to be the much cited one of Roberts, a missionary in the East Indies. According to his observation the early ovariotomy is followed by the disappearance of all sexual characters along with the prevention of the onset of puberty and the occurrence of menstruation. And in certain cases it is said resemblances to men appear. The value of the report is often doubted on the ground of uncertainty of the technique whereby the operation was carried out. But in considering the other reports scattered in the records it may be justifiable to say that early ovariotomy results in the degeneration of the whole genital apparatus and the secondary characters. In some even the opposite sexual signs may appear, beard, *e.g.* A loss of sexual feeling is agreed to be common (3, ii, p. 617).

When complete ovariotomy is carried out in later life, and this is not infrequently performed by gynecologists, the results are not so remarkable as those of the early cases. The cessation of menstruation, atrophy of the genital organs, internal and external, change of the voice to deeper and stronger are said to be the general effects.

Sometimes the appearance of hirsutism after castration has been described—a beard, hairy growth in the mammary and sternal regions (3, ii, p. 618). According to Vincent the sexual desire may not be affected by ovariotomy to any considerable degree, at any rate for some time, although he admitted the difficulty of obtaining exact information on this point (109, p. 304). Emotional disturbances usually follow ovariotomy as it is common at or around the menopause.

So far as the human subject is concerned, the foregoing statements have shown that the gonadal hormones play an important, if not vital, rôle in maintaining the physical sexual characters, and to some extent psychical, specific for each sex. The fact that this is due to the internal secretion of the sex glands did not receive our special attention in the previous discussion. Nevertheless, an incidental statement, made above, that the transplantation of the ovary in the abnormal part of the body of the animal which had been

subjected to ovariotomy will restore the normal "heat," affords an excellent instance of evidence for endocrine function of the ovary. The effect of the injection of the testicle extract which has also been already mentioned gives the same proof for the male glands.

There is heated discussion as to whether this gonadal hormone is elaborated in the germ cells, or, on the other hand, in the so-called interstitial cells. This, however, has no direct concern with our present problem, so reference must be made to the following recent writers—Harms (**45**), Stieve (**96**), and Lipschütz (**65**). The present tendency seems to favor the theory of interstitial cells. The interstitial cells are called by the name of puberty-glands (pubertätsdrüsen) by the Viennese school with Steinach as the leader. An interesting support, and what has a significant connection with our study, is afforded by Dr. Mott. He seems to consider the interstitial cells as the primary stimulus of the sexual desire, for he says:

"Possibly the persistence of the interstitial cells may account for an increased and perverted sexual appetite in old men, due to a stimulation of the desire without the power to perform the sexual act." (**75**, p. 658)

These statements were made on the basis of histological examination of the testicles from two aged senile dementia patients who died at the age of 85 and 86 respectively.

The Hyperfunction and Its Effect

So far our discussion has been confined to cases of diminished gonadal secretion. Since the gonadal hormone is not yet isolated, the result of extract injection must not be looked upon as identical with that of the endocrine action of the gonads. The well-known experiments of Brown-Séquard are, therefore, of historical significance.

Recently many experiments have been made attempting to call forth hypersecretion of the interstitial cells by the old method of occluding the vas deferens of the male internal genitals. That this operation causes degeneration and disappearance of the spermatozoa, while the interstitial tissue of the organ undergoes hypertrophy, was demonstrated years ago with various animals (**69**, p. 311). This has been utilized in man and it has been claimed rejuvenescence is attained. The basis is on the presupposition that an increased amount of the hormone is effected by the hypertrophy of the interstitial

tissue. The experiments on rejuvenescence by Steinach were so sensationally reported by newspapers and other periodicals that the ever-desired miracle seemed at last achieved. But, unfortunately, his and similar results by others have not been sufficiently established to command general acceptance.

Clinical symptoms, however, reveal the cases which are traceable to hypersecretion. When this occurs at an early age pubertas precox is the result.

We have already stated that pubertas precox is often associated with adrenal tumor, and that this in fact is the result of hyperfunction of a part originally derived from the testicular element. Many reports of this nature are in the literature. An interesting case of pubertas precox due to testicular tumor is the often quoted one of Sacchi. In a boy about five years of age it was noted that the left testicle began to increase in size. At nine he weighed 97 pounds, had hair on his lip and genitalia; voice deep, penis large, frequent erections, and seminal emissions. A tumor was found in the left testicle and the testicle was removed. Four months afterwards, the hair on the chin had disappeared, that on the upper lip and pubes persisted; the voice became infantile, the penis shrunk, erections, emissions and sexual impulses ceased (3, ii, pp. 350, 505).

An excellent example of a case of probably pure hyperfunction without tumor is reported by Stone (3, ii, p. 506). The parts most relative to our discussion will be quoted. A boy four years old showed the well proportioned muscular and osseous system of a perfectly developed miniature athlete of 21 years of age; abundant hair in the axilla and on the pubes, lumbar and sacral regions, 4 feet and ¼-inch height, weighed nearly 70 pounds; penis of man's size; testicles firm, well-developed, about the average size of an adult's. From the neck down the appearance was that of a perfect man, whilst the head and face were those of a child. The teeth only were deciduous. The boy was lively, and seemed intelligent, though his speech was imperfect, but he could pronounce with facility after his father. He was a little bashful before strangers. His temper was good, but when excited by anger his father alone could manage him, by a knock-down blow.

No sexual action had been known. The following information, however, was obtained from his father, which clearly reveals his sexual desire:

"On the 13th of September he slept with a near relative, a

married lady, the mother of several children. In the middle of the night, she was aroused by finding the boy closely clasped to her back, and her nightdress saturated. She thought he had emptied his bladder upon her, but on carrying her hand to the part, she found that it was saturated with a very different and glutinous material from that she expected."

The boy was extremely fond of embracing the opposite sex, though nothing further had been ascertained (**3**, ii, pp. 506–508).

Pubertas precox accompanied by tumor in the adrenal cortex is said to be more common in girls than in boys. But these girls, as already mentioned, are in reality cases of virilism, not pubertas precox. The examples of true precocious puberty in girls seem to be limited. One instance, however, is given by Harrow (**46**, p. 114). A girl of seven had already menstruated a number of times, and had well-developed breasts and pubic hair. A tumor of the ovary was removed, and the girl grew up into normal womanhood. It is greatly to be regretted that a description of her mentality is entirely missing in this case. Presumably it might have paralleled the physical development. (For another example see Biedl **6**, p. 257).

From the contrast of the foregoing examples with the results of castration above mentioned we are impressed with the fact that the hormones from the genital glands exert great influence on the mental activity of the human being, especially on the sexual desire or, in more refined terms, the love emotion, which is regarded by the Freudian school as the original driving motor of life, and the fundamental spring of the new life at the period of storm and stress.

The question whether the hormone of the genital gland from each sex has specific power in coloring and maintaining the specific sexual mental characters of the respective sexes may be too delicate to be answered from our meager present knowledge in more than a very limited degree.

The mental characteristics of the eunuchs above mentioned possibly serve as a part of the negative evidence for the present issue. Some positive proof has been furnished by the following experiments.

The effects of the cock's testicular extract on the physical appearance of normal hens are referred to by Marshall (**69**, p. 312). All male characters are said to have been developed in two hens after daily injection for several months, which returned to the original condition after it was discontinued. Many experiments of this

nature and in transplanting opposite sex glands have entailed similar results.

Recent experiments of Moore are of importance. Gonads from the opposite sex were implanted in the bodies of over 50 guinea pigs of both sexes, which had undergone complete castration at 10 to 20 days of age. Repeated grafts were made in many cases, when necessary. The ovarian grafts in the male led to hypertrophy of the nipples, while the grafts of testicles in the females brought about a remarkable enlargement of the clitoris. The mental characters of the female were so modified that the animals behaved like males: whereas the reverse effect was not observed in the males which retained their normal psychical characteristics (70).

Steinach, Sand and Moore are referred to by Wheelon (3, ii, pp. 458–459) as having made similar experiments. They have shown, contrary to the above results, that castrated males carrying the implanted ovary developed nervous reflexes normally peculiar to the female: " The tail erect reflex, and a kicking, guarding reflex to ward off the male before the appearance of heat. Moreover, they are sought by normal males as though they were females. The mother instinct to protect and nurse the young is also noticeable." No reference is made as to what was the experimental animal, presumably a dog. If so, the so-called female nervous reflexes are not so specific, and the seeking of the male as if it were female is by no means uncommon. " On the other hand, young female rats have been converted into such apparently mature males that they react psychically as males and imitate the normal male in a very exact way in the act of copulation." This accords with the experiment, previously referred to, by Moore.

Further, the combined influence of the male and female gonads produces hermaphrodites. Clinical and surgical reports on this subject are not uncommon. Sand succeeded in producing this artificially. Ovary and testicles were implanted in the abdominal wall of a young castrated male guinea pig on each side respectively. Penis and mammae developed, and milk was secreted from the latter. Psychosexually the animal showed the mixed type; passing in a course of an hour from a mild female to a violent male when put near a male, female or a new born animal (85).

From these observations we may safely say that the gonadal hormone performs a significant rôle in coloring, if not determining and maintaining, the specific sexual characters of the psychical process

as well as the physical one. Schäfer is correct in saying that, in substance, the female is female not only because she produces ova, but because she produces the ovarian secretion; while the male is male not only because he produces spermatozoa, but because he also possesses the testicular hormone (89, p. 351).

Finally, just a word should be mentioned about the nature of the gonadal hormone. On many occasions we have referred to the fact that the ovariotomy tends to develop in the females which have undergone castration the malelike characters, while castration in the male only leads to arrest of the male peculiarities. And, again, implantation and injection of the testicle substance produce in the female the development of male physical characters, and oftentimes even the assumption of the opposite psyche. These facts lead to the prevalent notion that the secondary male characters are normally present in a latent form in the female, and that the ovarian hormone exerts a restraining influence over their development.

This hypothesis seems to get further support since Mott has shown that while no evidence of maturation of germ cells is found in boys before puberty, sections of the ovaries of a female infant aged 18 months show complete Graafian follicles with the endocrine cells surrounding the follicles (72, pp. 10–11; 75, p. 656; 76, p. 283).

E. *The Parathyroid*

While the positive function of the parathyroid gland is rather obscure, the effect of its removal is exceedingly remarkable, especially since it manifests itself in the effect on the nervous system. The symptoms resulting from parathyroidectomy resemble those characterizing an affection common in infancy known as tetany, and accordingly are termed tetania parathyroid priva. These are said to vary in different animals, and in the same animal at different times. They are most severe in carnivorous animals such as dogs and foxes, especially in the young. In these animals the peculiar effects on the nervous system show themselves most clearly in muscular tremors and convulsions of a clonic character, passing eventually into fits, which after many alternating attacks and temporal recovery finally lead to death. Besides these symptoms are many other sympathetic and parasympathetic disturbances—quickened heartbeat, increase of salivation, itchiness of the mouth and lips, rapid breathing, rise of temperature, etc.

In dogs signs of restlessness and anxiety are observed after

parathyroidectomy (MacCallum), whereas in cats, the symptoms which are generally less marked than in dogs, are described as invariably those of depression and sluggishness (Paton and Findlay). These last mental conditions are considered by Paton and Findlay as the inevitable result of the removal of a sufficient amount of parathyroid tissue in various animals such as cats, dogs and monkeys; although the peripheral nerves are increased in their excitability (**3**, i, p. 529).

These symptoms described above are very remarkable, and it is astonishing that these tiny glands—one of the smallest independent organs of the body, collectively not weighing more than two grams with all four (very often 3, 2, or even only one is found in the human subject, see Kojima, **57**, p. 23)—should produce so serious a train of affects. And the results are thought to be elicited from the effect on the central nervous system, especially on the spinal nerves. The reason for the production of these symptoms is now generally believed to be the result of removal of antitoxic substance which the parathyroid normally furnishes to the blood.

Mechanism and Hygiene of Emotion

1. *Neuro-endocrine Mechanism of Emotion*

In strong emotion the entire sympathetic realm is called into action, and the parasympathetic innervation is suppressed. In anger, for example, the pupil is dilated, the heart-beat accelerated, the respiration quickened, blood pressure raised, hair erected, sweat profuse, the whole alimentary and genital activity checked, and the muscles tremble. Of course these striking somatic changes are all capable of being brought about by nervous action alone, but the previously mentioned facts show quite clearly that the endocrine substances play a significant part in these bodily changes reinforcing and prolongating the nervous operation. Thus chemical substances from adrenal (**35**), thyroid, and pituitary, act on the organism just as the sympathetic system does. Further, adrenalin is said to hasten blood-clotting and to abolish the effect of muscular fatigue (**14**). Recently pituitrin is claimed to have the latter effect (**106**). Increment of blood-sugar and subsequent glycosuria are known to be elicited by adrenalin, thyroid extract and perhaps by pituitrin. It is obvious, then, that some of the hormones reinforce nervous action in bringing about enormous bodily changes in time of great emotion. Some of the changes, pupil dilatation, etc., appear after a latent

period and persist after nervous stimulation has stopped. Coöperation of hormone with the nerve is presumable. The so-called post-emotional state or mood may be partially ascribed to the persisting hormonic action.

How is the neuro-endocrine mechanism operated when emotional agitation occurs? This is an extremely difficult question. The nervous center for emotional expression, mainly mimetic, is alleged by many investigators to exist in some part of the diencephalon (**49, 81, 82, 92, 118**). What relation this part of the brain has with the endocrine activities we do not know.

We know that the emotional expressions are not limited to the facial ones, that there are other grosser bodily changes, and that these others are activated predominantly by the sympathetic nervous system. Though the location of the sympathetic center is yet obscure, Edinger, Karplus and Kriedl describe it as lying in some point of the mid-brain (**3**, i, p. 162).

On the other hand, the reflex center whereby the adrenal secretion is controlled is determined by Elliot to exist in some part of the medulla oblongata, in the "neighborhood of the vasomotor center which governs other sympathetic musculature" (**36**, p. 407). Recently Cannon and Rapport came to the conclusion, from their elaborate experiments, that the reflex center for adrenal secretion is located immediately back of the corpora quadrigemina in the floor of the fourth ventricle (**22**, p. 34). Both experiments above referred to indicate that the reflex center of the adrenal body is somewhere in the mid-brain.

It is very suggestive for our present work to note that both the sympathetic center and the reflex center for the adrenal secretion are assigned to the mid-brain. More so, when we take into account, on the one hand, the facts that glycosuria is experimentally caused by puncture of the floor of the fourth ventricle, and that polyuria is supposed to have its center in the mid-brain; on the other hand, the fact that these phenomena appear with the emotional stress. Presumably the emotion arouses the endocrines directly through their nervous centers, and these centers lie in nearly the same area of the brain. Thus the normal emotional process is brought about and maintains itself through the neuro-endocrine mechanism.

2. Hygiene of Emotion

Emotion, as the name suggests, is agitation, or better, disintegrative or disruptive in nature. When it becomes intensive enough

the neuro-endocrine system is first mobilized and then the whole musculature. The whole organism is selectively prepared for ensuing bodily action. The activity of the alimentary canal is temporarily stopped, the blood is transferred from this part to the limbs, adrenalin increased and sugar called forth from the liver, the thyroid becomes more active, and the metabolic rate is heightened. In a word, emotion tends to provide the complete bodily condition to meet an emergency. It may be compared to the function of inflammation of organic tissue or to the military mobilization of the nation. The final aim is to restore the welfare of the organism or of the country. But the mobilization in case of emotion or of military power always means abnormality and disturbance. Like a nation after a war, the organism after an emotional storm becomes weak and exhausted. The so-called war-disease or war-psychosis is a concrete extreme example which illustrates the neuro-endocrine exhaustion after the overstimulation of emotion.

The continuous stimulation of strong emotion such as anger and fear will result in adrenal exhaustion and consequently in the overwork of the liver and thyroid and perhaps the pituitary. And the result of the overstimulation of the endocrines is evident from the previous statement. Cannon's experiment, performed on cats producing the symptoms of hyperthyroidism by connecting the secretory nerve of the thyroid with the phrenic nerve, should be recalled here. Emotional hyperglycosuria in man and animals, and the artificial hyperglycosuria produced by injection of adrenalin or the extract of the thyroid or pituitary, suggest the possible evil result of the prolonged emotional strain. Indigestion accompanying strong emotions is a no less important symptom, popularly known and experimentally proved, and often pointed out as a cause of various mental disorders.

Hammett's recent work is interesting in this connection. Parathyroids of the albino rats from two stocks, one tamed and gentle, the other untamed and hypertensive, were extirpated. The ratio of mortality after two days of the operation was studied with each stock. The percentage of mortality of the tamed was 13 and that of the other group, 76. "This definitely showed," says Hammett, "that the stability of the nervous system is a strong factor in the resistance of albino rats to the loss of the parathyroid secretion" (44, p. 201). The cause of the high mortality in the group of the emotional rats, as he called them, was ascribed to the "greater tendency to the formation of toxic compounds than is found in those rats of low

muscular tone." If we accept this explanation, hyperactivity of emotion causes a large production of toxic substances; and overfunction of the parathyroid is naturally demanded. The unhealthy influence of hypertension on the gland and thus on the whole organism, even if parathyroidectomy is not performed, is not hard to be seen.

The undesirable effect of strong emotion is not restricted to that on the somatic economy, but the mental activity is also affected, temporarily or permanently. Psychiatrists can tell of numberless cases of insanity caused by or at least related to the emotional story; the temporary "craziness" aroused by emotion is too well known to be mentioned.

Sexual emotion is very important in this connection. The exact neuro-endocrine mechanism of emotion regarding the gonads is obscure. The age of onset of various psychoses tells the important relation of the gonads to mental hygiene, especially the hygiene of emotion. Degenerative changes in the gland of dementia precox patients, both male and female, are found noted as an etiological factor by many authorities like Tiffany (**99**), Mott (**76**), and Abderhalden (**40**, a). The theory is still in dispute, but it suggests the close connection between the disease and these glands.

So far we have discussed only the unfavorable result of overstimulation of emotion. But understimulation of emotion is equally bad. The Freudian school strongly teaches us the morbid result of suppression of emotion. Emotion may be luxurious, as some say. Daily work may be duly performed in our community without a bit of emotion, as our life could be maintained on tasteless but chemically perfect foodstuff. But how miserable life would be! Normally the whole mental activity is more or less colored by an affective tone. Repression of normal emotion means a colorless mental world. We have mentioned the glycosuria accompanying depression of emotion.

We have seen that pleasant emotion is favorable to digestion. This is of great significance as regards mental hygiene. Very often indigestion causes various psychoses. The cessation of the digestive function in the case of strong emotion through the neuro-endocrine mechanism, above mentioned, has great importance in relation to the hygiene of emotion. Recently Dr. Cannon came to the conclusion as the result of his experiments, that the inhibitory nerve for the adrenal secretion is the vagus, and the center of it is in the mid-brain, nearly the same as the excitatory center (**22**). This is a very impor-

tant contribution. We know that the vagus is the secretory nerve for the salivary, gastric, and pancreatic glands (12, 79); in other words, the action of the vagus is favorable for food digestion. Thus, it may be stated considering the above that pleasant emotion stimulates the vagus nerve, producing a favorable condition for bodily construction, and it inhibits the adrenal secretion, thus checking a condition destructive for the organism. Looking upon emotion in its relation to digestion, it is evident, therefore, that pleasant emotions are healthful, and strong emotions, like fear, anger, are injurious. This holds true not only of the digestive function but also of the other bodily activities; and, further, for the mental health.

However, it should not be forgotten that even pleasurable emotion is unwholesome when it becomes too strong, as is shown by an example cited by Cannon (14, p. 277) and by our daily experience. Virtually fear and anger protect the organism not only in the natural life of the animal kingdom, but also in the human life of civilized society, if experienced in a mild degree. We can agree with Dr. Burnham when he postulates the principle of hygiene in the following words: "The maintenance of an optimum stimulation and reaction" (9, p. 365). "To maintain a condition of healthful function," he says elsewhere, "it is necessary to keep stimulation and response within certain limits; overstimulation, understimulation, overreaction, and lack of reaction, are alike injurious to health" (9, p. 330).

Certain endocrinologists attempt to associate a specific emotion with a special ductless gland—pituitary with fear anxiety; adrenal with courage, for example. It would be a great invention if we found the way to regulate a man's particular emotion and his character by extract administration, transplantation, or partial removal of the endocrines. All the endocrines, however, like other organs, are complexly interrelated with one another in their function; and accordingly in their relation to the mental activity there exists also an intricate correlation. We can hardly attach any specific emotion to a specific endocrine; and so the regulation of the emotional activity is only possible through lowering or heightening of the mentality as a whole; as is seen in the case of thyroidal administration to cretins. The only way to control a specific emotion so as to maintain mental and somatic health is to control the stimulation of the emotion, by biologically adequate stimuli or by individually acquired conditioned stimuli. For the details of the practical method another study is required.

Bibliography

1. Anrep, G. V., The Augmented Salivary Secretion. *J. of Physiol.*, 1922, **56**, 263–268.
2. Barker, L. F., Remarks on the functions of the supra-renal glands as revealed by clinical, pathological studies of human beings and by experiments on animals. *Endocrinol.*, 1919, **3**, 253–261.
3. Barker, L. F., *Endocrinology and Metabolism.* N. Y. Appleton, 1922, 5 vols.
4. Bell, C., *The Anatomy and Physiology of Expression as Connected with the Fine Arts.* London, 1885, 254.
5. Bercovitz, Z., Preliminary report on the effects of vagus stimulation on the dog's stomach and the influence of asphyxia on these effects. *Proc. Soc. for Exper. Biol. & Med.*, 1922, **19**, 228–230.
6. Biedl, A., *Innere Sekretion.* Berlin & Wien. 1913, 2nd ed., 2 vols.
7. Biedl, A., Ueber die Hypophysis. *Klin. Wochenschr.* 1922, **1**, 1280.
8. Borberg, N. C., Histologische Untersuchungen der Endocrine Drüsen bei Psychosen. *Arch. f. Psychiat. u. Nervenkrankheiten.* 1921, **63**, 391–402.
9. Burnham, W. H., The Fundamental Principle of Hygiene. *Ped. Sem.* 1918, **25**, 329-368.
10. Cameron, A. T., Thyroid Function from a Chemical Viewpoint. *Canada Med. Assoc. J.* 1922, **12**, 229–232.
11. Camus, J. & Roussy, G., Experimental researches on the pituitary body. Diabetes insipidus, glycosuria and those dystrophies considered as hypophyseal in origin. *Endocrinol.* 1920, **4**, 507–522.
12. Cannon, W. B., *The Mechanical Factors of Digestion.* London & N. Y. 1911, 227.
13. Cannon, W. B., The Interrelations of Emotions as Suggested by Recent Physiological Researches. *Am. J. of Psychol.*, 1914, **25**, 256–282.
14. Cannon, W. B., *Bodily Changes in Pain, Hunger, Fear and Rage.* London & N. Y., 1915, 311.
15. Cannon, W. B., The Isolated Heart as an Indicator of Adrenal Secretion Induced by Pain, Asphyxia and Excitement. *Am. J. Psychiat.*, 1922, **2**, 15–30.
16. Cannon, W. B., New Evidence for Sympathetic Control of Some Internal Secretions. *Am. J. Psychiat.*, 1922, **2**, 15–30.
17. Cannon, W. B., Invitations to Research in Endocrinology. *Endocrinol.*, 1922, **6**, 745–759.
18. Cannon, W. B., & Cattell, J. McK., The Electrical Response as an Index of Glandular Action. *Am. J. of Physiol.*, 1916, **41**, 39–57.
19. Cannon, W. B., & Cattell, J. McK., The Secretory Innervation of the Thyroid Gland. *Am. J. of Physiol.*, 1916, **41**, 58–73.
20. Cannon, W. B., & Cattell, J. McK., The Influence of the Adrenal Secretion on the Thyroid. *Am. J. of Physiol.*, 1916, **41**, 74–78.
21. Cannon, W. B., & Rapport, D., Further Observations on the Denervated Heart in Relation to Adrenal Secretion. *Am. J. of Physiol.*, 1921, **58**, 308–337.

22. Cannon, W. B., & Rapport, D., The Reflex Center for Adrenal Secretion and Its Response to Excitatory or Inhibitory Influences. *Am. J. of Physiol.*, 1921, **58**, 338–382.
23. Cannon, W. B., & Uridil, W. E., Some Effects on the Denervated Heart of Stimulation of the Nerves of the Liver. *Am. J. of Physiol.*, 1921, **58**, 353–364.
24. Cannon, W. B., & Smith, P. E., Further Evidence of Nervous Control of Thyroid Secretion. *Am. J. of Physiol.*, 1922, **60**, 476–494.
25. Cannon, W. B., & Griffith, F. R., Cardiac Accelerator Substance Produced by Hepatic Stimulation. *Am. J. of Physiol.*, 1922, **60**, 544–559.
26. Cannon, W. B., & Carrasco-Formiguera, R., Reflex and Asphyxial Secretion of Adrenalin. *Am. J. of Physiol.*, 1922, **61**, 213–227.
27. Carlson, A. J., Rooks, J. R., & McKie, J. F., Attempts to Produce Experimental Hyperthyroidism in Mammals and Birds. *Am. J. of Physiol.*, 1912, **30**, 129–159.
28. Carrasco-Formiguera, R., The Production of Adrenal Discharge by Piqûre. *Am. J. of Physiol.*, 1922, **61**, 254–271.
29. Crile, G. W., *The Origin and Nature of the Emotions.* Phila. & Lond. 1915, 240.
30. Crile, G. W., *Man, an Adaptive Mechanism.* 1916, N. Y. 387.
31. Cushing, H., Psychic Disturbances Associated With Disorders of the Ductless Glands. *Am. J. Insanity.*, 1913, **69**, 963–990.
32. Dana, C. L., The Anatomic Seat of the Emotions; a Discussion of the Lange-James Theory. *Arch. of Neur. and Psychiat.*, 1921, **6**, 634–639.
33. Darwin, C., *The Expression of the Emotions in Man and Animals.* 1873, N. Y., 374.
34. Duchenne de Boulogne, *Mécanisme de la physionomie humaine.* 2nd ed. 1876, Paris, 196.
35. Elliot, T. R., On the Action of Adrenalin. *J. Physiol.*, 1905, **32**, 401–467.
36. Elliot, T. R., The Control of the Suprarenal Glands by the Splanchnic Nerves. *J. Physiol.*, 1912, **44**, 374–409.
37. Elliot, T. R., Ductless Glands and the Nervous System. *Brain*, 1912-13, **35**, 306–321.
38. Elliot, T. R., The Innervation of the Adrenal Glands. *J. Physiol.*, 1913, **46**, 283–290.
39. Elliot, T. R., Some Results of Excision of the Adrenal Glands. *J. Physiol.*, 1914, **49**, 38–53.
40. Endocrinology, (a) The Pathogenesis of the Neuroses. *Endocrinol.*, 1917, **1**, 401–403. (b) 1923, **7**, 215.
41. Fay, D. W., A Psychoanalytic Study of Psychoses with Endocrinoses. N. Y., 1922, 122.
42. Gley, E., The Problem of the Adrenals. *N. Y. Med. J.*, 1921, **114**, 9–11.
43. Hall, G. S., A Study of Anger. *Am. J. Psychol.*, 1899, **10**, 516–591.
44. Hammet, F. S., The Stability of the Nervous System as a Factor in the Resistance of the Albino Rat to the Loss of the Parathyroid Secretion. *Am. J. of Physiol.*, 1921, **56**, 194–204.
45. Harms, W., Keimdrüsen und Alterzustand. *Fortschr. d. Naturwissensch. Forsch.*, 1922, **77**, 189–198.

46. HARROW, B., *Glands in Health and Disease.* N. Y., 1922, 218.
47. HARTMAN, F. A., MCCORDOCK, H. A., & LODER, M. M., Conditions Determining Adrenal Secretion. *Am. J. of Physiol.*, 1923, **64**, 1–34.
48. HARTMAN, F. A., MCCORDOCK, H. A., & LODER, M. M., The Emergency Function of the Adrenals. *Science*, 1922, **56**, 146–147.
49. HEAD, H., & HOLMES, G., Sensory Disturbances from Cerebral Lesions. *Brain*, 1911-12, **34**, 102–254.
50. HENDERSON, D. K., Anxiety States Occurring at the Involutional Period. *J. Ment. Sci.*, 1920, **66**, 274–282.
51. HOSKINS, R. G., Some Recent Work on Internal Secretions. *Endocrinol.*, 1922, **6**, 621–632.
52. HOUSSAY, B. A., Rôle de l'adrénalin dans les effects hypertensifs produit par excitation du nerf splanchnique ou par piqure bulabaire. *Compt. Rend. Soc. de Biol.*, 1922, **87**, 695–698.
53. HOWELL, W. H., *A Textbook of Physiology.* Phila., 1922, 8th ed. rev., 1053.
54. JAMES, W., *The Principles of Psychology.* N. Y., 1890, 2 vols.
55. JANNEY, N. W., Concerning the Pathogenesis of Thyrotoxicocis. *Endocrinol.*, 1922, **6**, 795–810.
56. KEMPF, E. J., *Autonomic Functions and the Personality.* N. Y. and Wash., 1921, 156.
57. KOJIMA, M., The Ductless Glands in 110 Cases of Insanity, with Special Reference to Hypothyroidism. *Proc. Roy. Soc. Med.*, 1915, **8**, Sect. Psychiat., 21–57.
58. KOJIMA, M., Studies on Endocrine Organs of Dementia Praecox. *Proc. Roy. Soc. Med.*, 1917, **10**, 88–89.
59. KOOY, F. H., Hyperglycemia in Mental Disorders. *Brain*, 1919, **42**, 214–289.
60. KRABBE, K. H., The Relation Between the Adrenal Cortex and Sexual Development. *N. Y. Med. J.*, 1921, **114**, 4–8.
61. LADD, G. T., & WOODWORTH, R. S., *Elements of Physiological Psychology.* N. Y., 1911, rev. ed., 704.
62. LEVY, R. L., The Effect of Thyroid Secretion on the Pressor Action of Adrenin. *Am. J. of Physiol.*, 1916, **41**, 492–511.
63. LEWIS, N. D. C., *The Constitutional Factors in Dementia Precox.* 1923. Nerv. and Ment. Dis. Pub. Co., N. Y., 134.
64. LIPSCHÜTZ, A., OTTOW, B., & WAGNER, K., Ueber das Minimum der Horden-substanz, das für die normale Gestaltung der Geschlechtsmerkmale ausreichend ist. *Arch. f. d. ges. Physiol.*, 1921, **188**, 76–86.
65. LIPSCHÜTZ, A., New Experimental Data on the Question of the Seat of the Endocrine Function of the Testicle. *Endocrinol.*, 1923, **7**, 1–18.
66. MACKENZIE, H., Exophthalmic Goitre. *Lancet*, 1916, 815–821.
67. MAEVSKI, W. E., The Part Played by the Sympathetic Nerve in Salivary Secretion. *Russ. J. of Physiol.*, 1922, **4**, 1–18.
68. MARANÓN, G., La reaction emotiva á la adrenalina. *Med. Ibra* (Madrid), 1920, **145**, 353–357. (*Endoc.*, 1921, **5**, 97–99.)
69. MARSHALL, F. H. A., *The Physiology of Reproduction.* N. Y., 1910, 706.

70. Moore, C. R., On the Physiological Properties of the Gonads as Controllers of Somatic and Psychical Characteristics. IV. Gonad Transplantation in Guinea-Pig. *J. Exper. Biol.*, 1921, **33**, 365–391.
71. Mosso, A., The Mechanism of Emotions. *Clark Univ. Decennial Celebration*, 1899, 396–407, Worcester, Mass.
72. Mott, F. W., The Application of Physiology and Pathology to the Study of the Mind in Health and Disease. *Proc. Roy. Soc. Med.*, 1915, **8**, Sect. Psychiat., 1–16.
73. Mott, F. W., Microscopic Examination of the Central Nervous System in Three Cases of Spontaneous Hypothyroidism in Relation to a Type of Insanity. *Proc. Roy. Soc. Med.*, 1915, **8**, 58–70.
74. Mott, F. W., The Changes in the Central Nervous System in Hypothyroidism. *Proc. Roy. Soc. Med.*, 1917, **10**, 51–59.
75. Mott, F. W., Normal and Morbid Conditions of the Testes from Birth to Old Age in One Hundred Asylum and Hospital Cases. *Brit. Med. J.*, 1919, **2**.
76. Mott, F. W., The Psychopathology of Puberty and Adolescence. *J. Ment. Sci.*, 1921, **67**, 279–318.
77. Murdock, J. M., Endocrine Disturbance in Mental Defectives. *Penna. Med. J.*, 1921, **25**, 50.
78. Naccarati, S., Hormones and Emotions. *Med. Record*, 1921, **99**, 910-915.
79. Pavlov, I. P., *The Work of the Digestive Glands*. Tr. by W. H. Thompson. 2nd Engl. ed., 1910, London, 266.
80. Pende, N., Endocrinopathic Constitutions and Pathology of War. *Endocrinol.*, 1919, **3**, 329–341.
81. Pillsbury, W., *The Fundamentals of Psychology*. Rev. ed., 1922, N. Y., 589.
82. Prideaux, E., Expressions of Emotion in Cases of Mental Disorder as Shown by the Psychogalvanic Reflex. *Brit. J. Psychol., Med. Sect.*, 1921, **2**, 3–46.
83. Rothacker, A., Hyperthyroidism bei Kriegsteilnehmen, Neurogenen Entstehung dieser Krankheit. *Münch. med. Wchnschr.*, 1916, 63, 99.
84. Rutherford, H. R. C., Insanity and Endocrine Glands. *Brit. Med. J.*, 1922, **1**, 581.
85. Sand, K., De l'hermaphrodisme expérimentale. *Compt. Rend. Soc. de Biol.*, 1922, **86**, 1017-1024.
86. Shamoff, V. N., Concerning the Action of Various Pituitary Extracts upon the Isolated Intestinal Loop. *Am. J. of Physiol.*, 1915-16. **39**, 268–278.
87. Shamoff, V. N., On the Secretory Discharge of the Pituitary Body Produced by Stimulation of the Superior Cervical Sympathetic Ganglion. *Am. J. of Physiol.*, 1915–16, **39**, 279–290.
89. Schäfer, E. A., *The Endocrine Organs*. 1916, London, 156.
89. Schäfer, E. A., The Influence of the Internal Secretions on the Nervous System. *J. Ment. Sci.*, 1922, **68**, 347–367.
90. Shand, A. F., *The Foundations of Character*. London, 1920, 578.
91. Sherrington, C. S., Experiments on the Value of Vascular and Visceral Factors for the Genesis of Emotion. *Proc. Roy. Soc.*, 1900, **66**, 390–403.

92. SHERRINGTON, C. S., *Integrative Action of the Nervous System.* N. Y., 1906, 411.
93. STEWART, G. N., & ROGOFF, J. M., The Alleged Relation of the Epinephrin Secretion of the Adrenals and Certain Experimental Hyperglycemias. *Am. J. of Physiol.*, 1917, **44**, 543–580.
94. STEWART, G. N., & ROGOFF, J. M., The Relation of the Epinephrin Output of the Adrenals to Changes in the Rate of the Denervated Heart. *Am. J. of Physiol.*, 1920, **52**, 304–363.
95. STEWART, G. N., & ROGOFF, J. M., Essentials in Measuring Epinephrin Output with Further Observations in Its Relation to the Rate of the Denervated Heart. *Am. J. of Physiol.*, 1920, **52**, 521–561.
96. STIEVE, H., Neue Untersuchungen über die Zwischenzellen. *Anat. Anz.*, 1921, **54**, 63–74.
97. STODDARD, W. H. B., The Rôle of the Endocrines in Mental Disorders. *Am. J. Psychiat.*, 1922, **2**, 374–378.
98. TIDY, H. L., Dyspituitarism. *Lancet*, 1922, 597–602.
99. TIFFANY, W. J., The Pathological Changes in the Testes and Ovaries in Dementia Praecox. *State Hosp. Quart.*, N. Y., 1920-21, **6**, 159–166.
100. TOURNADE, A., & CHABROL, M., Double mécanisme, glycoet adrénalino-secrétoire de l'hyperglycémie par excitation splanchnique. Dissociation expérimentale. *Compt. Rend. Soc. de Biol.*, 1922, **86**, 315–316.
101. TOURNADE, A., & CHABROL, M., Précisions sur le rôle vaso-constricteur par attribué au splanchnique. *Compt. Rend. Soc. de Biol.*, 1922, **86**, 775–776.
102. TOURNADE, A., & CHABROL, M., L'adrenalinemie consecutive à l'excitation du splanchnique temoigne bien d'une activité sécrétoire des surrenales, regie par le système nerveux. *Compt. Rend. Soc. de Biol.*, 1922, **86**, 776-778.
103. TOURNADE, A., & CHABROL, M., Le procés de l'adrenalinémie physiologique; le pour et le contre. *Compt. Rend. Soc. de Biol.*, 1922, **86**, 778–780.
104. TUCKER, B. R., The Internal Secretions in Their Relationship to Mental Disturbance. *Am. J. Psychiat.*, 1922, **2**, 259–270.
105. UNO, T., Effect of General Excitement and of Fighting on Some Ductless Glands of Male Albino Rats. *Am. J. of Physiol.*, 1922, **6**, 203-214.
106. URECHIA, Pituitrin and Muscular Fatigue. *Endocrinol.*, 1923, 181.
107. VAN DYKE, H. B., The Effect of Stimulation of the Vago-Sympathetic Nerve on the Distribution and Concentration of Iodine in the Dog's Thyroid Gland. *Am. J. of Physiol.*, 1921, **56**, 168-181.
108. VINCENT, S., Recent Views as to the Function of the Adrenal Bodies. *Endocrinol.*, 1917, **1**, 147-149.
109. VINCENT, S., The Endocrine Functions of the Female Reproductive Organs. *Lancet*, 1922, **2**, 303-305.
110. VINCENT, S., Current Views on Internal Secretion. *Lancet*, 1922, **2**, 313–320.
111. WARD, J., *Psychological Principles.* Cambridge, 1918, 478.
112. WARREN, H. C., *Human Psychology.* Boston and N. Y., 1920, 460.
113. WATSON, J. B., *Psychology from the Standpoint of a Behaviorist.* Phila. and London, 1919, 429.

114. WEBER, E., *Der Einfluss psychologischer Vorgänge auf der Körper.* 1910, Berlin, 426.

115. WITTE, F., Ueber anatomische Untersuchungen der Schilddrüse bei der Dementia Praecox. *Zeit. f. d. ges. Neur. u. Psychiat.*, 1922, **80**, 190–199.

116. WUNDT, W., *Gründzuge der Physiologischen Psychologie.* 6th ed., 1911, 3 vols., Leipzig.

117. WUNDT, W., *Völker-Psychologie.* Vol. 1. Die Sprache, pt. 1, 3rd ed., 1911, Leipzig, 695.

118. ZANICHELLE, N., *Biologia della vita emotiva. Vito Maria Buscaino* (Bologne), 1921. *Endocrinol.*, 1922, **6**, 270-271.

110. ZIEHEN, *T., Leitfaden der physiologischen Psychologie.* 10th ed., Jena, 1914, 504.

Submitted for publication, April, 1924.

BOOKS RECEIVED

PIERCE, EDGAR, *The Philosophy of Character.* Cambridge: Harvard Univ. Press, 1924. xi+435.

SUTHERLAND, EDWIN H., *Criminology.* Philadelphia: Lippincott, 1924. Pp. 643.

LEVINE, ISRAEL, *Reason and Morals. An Enquiry Into the First Principles of Ethics.* Glasgow: Maclehose, Jackson, 1924. Pp. xi+177.

FRANKLIN, EDWARD E., *The Permanence of the Vocational Interests of Junior High School Pupils.* Johns Hopkins Stud. in Educ., No. 8, 1924. Pp. vii+61.

MOORE, THOMAS V., *Dynamic Psychology.* Philadelphia: Lippincott, 1924. Pp. viii+444.

(British) Board of Education. *Report of the Consultative Committee on Psychological Tests of Educable Capacity and Their Possible Use in the Public System of Education.* London: H. M. Stationery Office, 1924. Pp. xii+248.

BHAGAVAN DAS, *The Science of the Emotion.* 3d Ed. Madras: Theosophical Pub. House, 1924. Pp. 556.

SINGER, EDGAR A., JR., *Mind as Behavior and Studies in Empirical Idealism.* Columbus, R. G. Adams, 1924. Pp. ix+301.

FREUD, SIGM., *Collected Papers.* Vol. I. London: Hogarth Press, 1924. Pp. 359.

SELZ, OTTO, *Ueber die Persönlichkeitstypen und die Methoden ihrer Bestimmung.* Jena: Fischer, 1924. Pp. 44.

KRUEGER, FELIX, *Der Strukturbegriff in der Psychologie.* Jena: Fischer, 1924. Pp. 26.

ZIEHEN, TH., *Leitfaden der Physiologischen Psychologie in 16 Vorlesungen.* 12th Ed. Jena: Fischer, 1924. Pp. 653.

FELEKY, ANTOINETTE, *Feelings and Emotions.* New York: Pioneer, 1924. Pp. xv+245.

WALLIN, J. E. WALLACE, *The Education of Handicapped Children.* Boston: Houghton Mifflin, 1924. Pp. xiv+394.

KANTOR, J. R., *Principles of Psychology.* New York: Knopf, 1924. Pp. xix+473.

THURSTONE, L. L., *The Nature of Intelligence.* New York: Harcourt, Brace, 1924. Pp. xvi+167.

NOTES AND NEWS

DR. WALTER S. HUNTER has resigned as professor of psychology at the University of Kansas to take the G. Stanley Hall Chair of Genetic Psychology at Clark University.

THE death is announced of George Stuart Fullerton on March 23.

AT Syracuse University, Dr. Hulsey Cason has been promoted from assistant professor to associate professor of psychology.

DR. HOMER BISHOP, instructor in psychology at Cornell University, has been appointed assistant professor of psychology at Smith College.

DRS. GRACE M. FERNALD and Shepherd Ivory Franz, of the Department of Psychology, University of California, Southern Branch, Los Angeles, have organized an experimental school for speech and motor defects, and for limited children, especially the so-called mentally blind who seem unable to learn to read or spell. With Drs. Kate Gordon and Ellen B. Sullivan, they have also organized an out-patient clinic at the Children's Hospital, Hollywood, for psychological testing and for speech and motor training.

PROFESSOR W. W. CHARTERS, of the University of Pittsburgh, has been appointed professor of education in the University of Chicago.

JAMES WARD, professor of mental philosophy at Cambridge University, died on March 4, aged eighty-two years.

DR. PAUL S. ACHILLES has been appointed field representative and assistant to the director of the Personnel Research Federation, New York City.

ON February 1–3, commemorative exercises and conferences in genetic psychology were held at Clark University in memory of G. Stanley Hall and E. C. Sanford.